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MAY 1953
VOLUME 85 NUMBER 5

Published Monthly by
AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET • CHICAGO 10, ILLINOIS

Entered as Second Class Matter Jan. 4, 1911, at the Postoffice at Chicago, Under the Act of March 3, 1879. Annual Subscription, $12.00

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Communications regarding subscriptions, reprints, etc., should be addressed, A. M. A. AMERICAN JOURNAL OF DISEASES OF CHILDREN, American Medical Association, 535 North Dearborn Street, Chicago 10.

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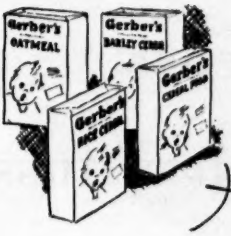

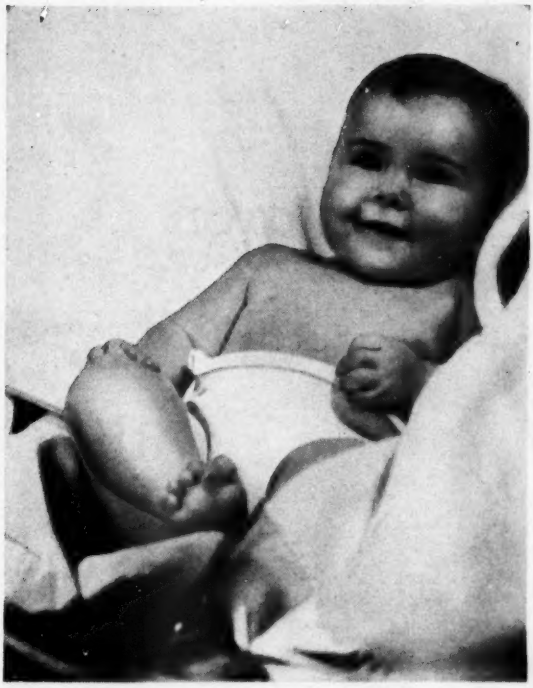

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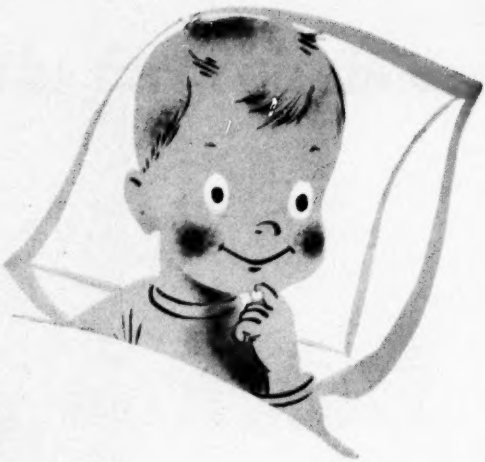

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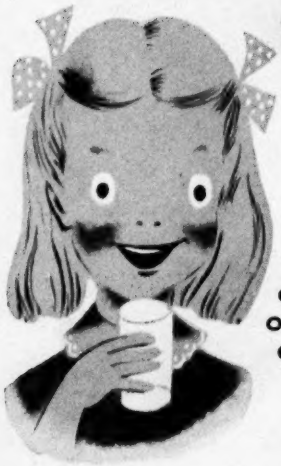

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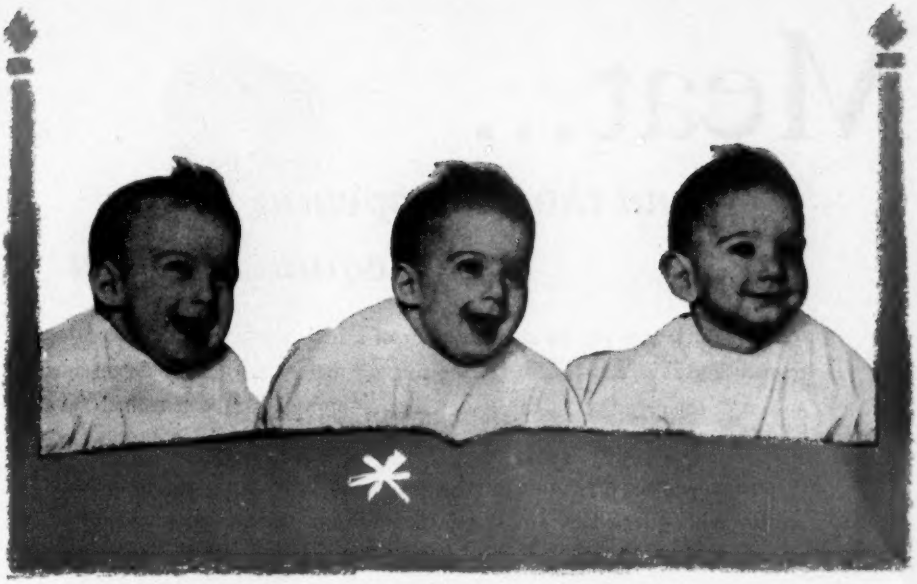

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*Sobel, S. H.: Milk Allergy in a case of Triplets, *Clin. Med.*, August 1952.

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American Journal of Diseases of Children

VOLUME 85 MAY 1953 NUMBER 5

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OVARIAN AGENESIS (CONGENITAL APLASTIC OVARIES) IN CHILDREN

HENRY K. SILVER, M.D.
NEW HAVEN, CONN.
AND
CHARLES HENRY KEMPE, M.D.
SAN FRANCISCO

OVARIAN agenesis (congenital aplasia of the ovaries) usually is associated with short stature, multiple congenital abnormalities, sexual infantilism, and high urinary gonadotropins. Although shortness of stature may be present from early childhood, the diagnosis of ovarian agenesis has seldom been made until after the age of puberty, when sexual infantilism calls attention to the related gonadal deficiency. However, Silver [1] has reported a complete study of a proved case with the characteristic signs of the syndrome in which elevated levels of urinary gonadotropins were found at the age of 2 years 8 months. The diagnosis was confirmed when exploratory laparotomy and biopsy of an ovary disclosed aplasia of these organs associated with a rudimentary uterus.

Besides Silver's case of ovarian agenesis in a prepubertal girl, other studies before the age of 14 years included one reported by van Creveld and de Vaal,[2] who have observed "a girl of 5 years old showing a complex of symptoms present in cases of ovarian agenesia. There was no enlarged excretion of gonadotropins such as is typical for the disease after puberty has been reached." Complete clinical or microscopic findings were not presented. Goldman and associates,[3] have described an 8-year-old girl with shortness of stature, coarctation of the aorta, and abnormalities of the toes. No endocrine studies were reported, and, although the patient died at the time of operation for correction of the cardiac defect, no data were given regarding the ovaries.

Kaijser [4] described a 10-year-old girl with definite cubitus valgus, webbed neck, hypertension, normal bone age, and moderate osteoporosis. Only one assay of gonadotropins was reported, and that was less than 40 mouse units per liter. On examination the uterus was found to be hypoplastic with a cord-like rudimentary

From the Division of Pediatrics, University of California School of Medicine, San Francisco.

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4. Kaijser, K.: Sexual Infantilism with Rudimentary Ovaries, Acta endocrinol. **3**:351, 1949.

ovary which histologically showed a cortical zone without any primary follicles. Marie and associates,[5] studied a girl between the ages of 13 and 14 years. She had shortness of stature, suggestion of hypertelorism, webbing of the neck, a short systolic murmur, "voluminous thorax," slender hips, and excellent muscular development. The clitoris was well developed, but the genital organs were infantile. She had an occasional pigmented nevus on the extremities. Some osteoporosis was noted on roentgenograms. The urine was positive at 25 mouse units for gonadotropins and negative at 50 mouse units. A rudimentary uterus was found at exploratory laparotomy, and the ovaries were elongated whitish structures. Wilkins [6] reported a 3-year-old girl with dwarfing, asymmetry of face, webbed neck, and coarctation of the aorta, in whom the follicle-stimulating hormone was less than 3 mouse units per day, but for whom the diagnosis of ovarian agenesis was confirmed by laparotomy. To date, Silver's case is the only one in which increased urinary levels of gonadotropins were found prior to the age of puberty.

The purpose of this paper is to present two additional cases of ovarian agenesis in prepubertal girls with short stature in whom elevated gonadotropins were found at 8 years 10 months and 12 years 5 months, respectively. A summary of the previously reported case is added in order to demonstrate other characteristic manifestations of the syndrome.

REPORT OF CASES

CASE 1.—J. J. was born in San Francisco on Nov. 6, 1938, weighing 6 lbs. 8 oz. (2,950 gm.) and measuring 19 in. (48 cm.) in length. She was referred to the University of California Hospital in April of 1951, at the age of 12 years 5 months, because of shortness of stature.

The mother had died within a few hours after the child's birth because of pulmonary embolism, and the father had been told that the child was "ill" during the first week of life, but the exact type of illness was not known. As far as he could recollect, the child had been small during the first six months of life, but no exact measurements were obtainable.

At the age of 6 months, she was moved to Minnesota, where, for the following seven years, she was cared for by a grandmother. On returning to California, at the age of 7 years, she weighed 39 lbs. (17.7 kg.) and was 41 in. (104 cm.) tall. Within the next few months she contracted chicken pox, mumps, measles, tonsillitis, and had many upper respiratory infections with an almost continual nasal discharge. Subsequently her health had been excellent.

The father was 38 years old and was 5 ft. 10 in. (178 cm.) tall. The mother had been 5 ft. 2 in. (158 cm.) tall. One paternal grandaunt and one granduncle, both of whom were not married, were "very short." The grandparents were said to be of average height or taller.

Physical examination revealed a well-developed stocky muscular girl who weighed 66½ lbs. (30 kg.) and was 50 in. (127 cm.) tall. She was active, alert, and intelligent and had a bright look; her cheeks were rosy, and her skin had normal turgor, texture, and moisture. The hair was normal. Twenty-eight permanent teeth were present. There was no webbing of the neck. No breast development had occurred. The nipples were widely spaced. The chest had a "shield shape" and was stocky. The heart was entirely clear to percussion and auscultation. Genitalia were infantile, with no pubic hair present. The femoral pulsations were strong. Blood pressure was 100/65. There was a tendency toward a hammer-toe deformity of the feet. She was seen by the ophthalmology consultant on June 22, 1951, and no ocular pathology was reported.

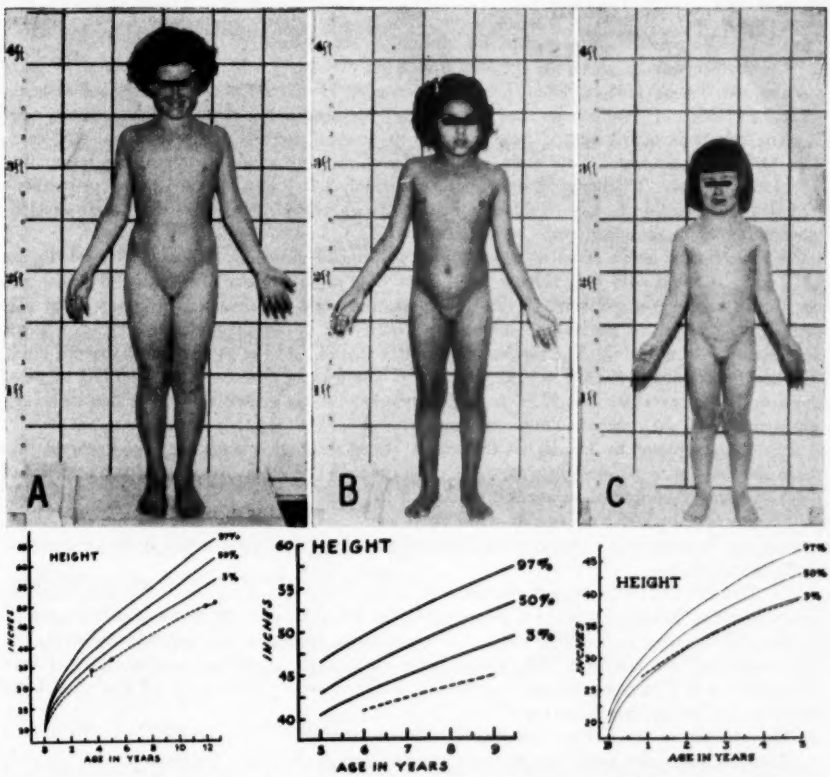
Dr. Ralph C. Benson, the gynecologic consultant, reported that the cervix uteri was a discrete, tubular structure approximately 2.5 cm. in length. A definite incisura was noted at the fundus, but no bicornate structure was felt. There was a small 1.5 cm. flattish body, free and

5. Marie, J.; See, G.; Barcat, J. R., and Pette, F.: Présentation d'une enfant atteinte de maladie de Turner-Albright, Arch. franç. pédiat. **7**:153, 1950.

6. Wilkins, L.: The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence, ed. 1, Springfield, Charles C Thomas, Publisher, 1950.

mobile, on the left, interpreted to be the left ovary. He could not be certain of the presence or absence of the right ovary on rectal examination alone. His impression was that of marked genital hypoplasia with a question of an ovarian vestige.

Roentgenograms for bone age showed that it was approximately 11 years. Generalized mild osteoporosis was present. The metacarpal bones were quite short, as were the phalanges. Roentgenograms of the teeth showed abnormally short roots; roentgenograms of the thoracic and lumbar spine disclosed no definite disease except for spina bifida of the first sacral vertebra. No abnormality of the skull was noted.



Photographs and growth curves (Stuart, H. C., and Stevenson, S. S., in Mitchell-Nelson: Textbook of Pediatrics, ed. 5, edited by W. E. Nelson, Philadelphia, W. B. Saunders Company, 1950, p. 59) of patients with ovarian agenesis; *A* (Case 1), age 12 years 5 months; *B* (Case 2), age 8 years 10 months; *C* (Case 3), age 4 years 9 months.

A 24-hour urine specimen was positive at 80 mouse units for gonadotropins.[7] A subsequent 24-hour urine specimen was positive at 160 mouse units and negative at 200 mouse units per 24 hours.

The reaction to Wassermann and Kahn tests was negative.

Assay of a 24-hour urine sample showed a 17-ketosteroid excretion of 0.81 mg. per 24 hours.

7. By this method normal adult women have been found to excrete between 5 and 80 mouse units per 24 hours, and no normal child under the age of 6 years has excreted as much as 5 mouse units. Studies on the excretion of gonadotropins by normal children are now under way.

Blood serum calcium was 11.1 mg. per 100 cc.; phosphorus, 4.9 mg. per 100 cc.; basic phosphatase, 13 units, and total protein 7.3 gm. per 100 cc. The blood examination revealed hemoglobin 11.5 gm. per 100 cc.; white blood cell count 7,500, and a normal differential count. The routine urinalysis was entirely within normal limits.

CASE 2.—L. M. was born in Nicaragua on Aug. 8, 1942, weighing 7 lbs. (3,175 gm.). She was raised in that country and was referred to the University of California Hospital in June, 1951, at the age of 8 years 10 months because of shortness of stature.

The mother believed her to be of normal length at birth, and dates the child's shortness of stature to one year of age. At 4 days of age and for the next 18 months, this child had repeated episodes of fever and diarrhea, which were reportedly due to malaria and typhoid fever. She received antimalarial therapy, but continued to have other attacks of malaria to the age of 7 years. Various purgatives were given for infestation with "worms."

The mother was 35 years old and was 5 ft. 2 in. (157 cm.) tall. The father was 45 years old and 5 ft. 5⅛ in. (165 cm.) tall. Two brothers, aged 12 (5 ft. 3 in. [160 cm.]) and 14 years (5 ft. 5 in [165 cm.]), were taller than average for Nicaraguan boys of their ages. A sister, aged 2 years, was of normal height. Three maternal great-aunts were short (4 ft. 11 in. [150 cm.], 4 ft. 11 in. [150 cm.], and 5 ft. ⅛ in. [152 cm.], respectively) while a paternal great-aunt was 5 ft. (152 cm.) tall. The maternal grandmother was only 4 ft. 9 in. (145 cm.) tall. The mother's half-sister was unable to have children for an unknown reason. However, her breast development is said to be normal.

Physical examination revealed a well-developed stocky muscular girl who weighed 48 lbs. (21.8 kg.) and was 44½ in. (113 cm.) tall. Her head circumference was 20 in. (51 cm.) and chest circumference was 25 in. (64 cm.). She was alert and intelligent. There was racial pigmentation and marked generalized hirsutism. There was no webbing of the neck. No breast development had occurred. The nipples were widely spaced, and she had a "shield-shaped" chest. The heart was normal. Genitalia were infantile. There was an increase of the carrying angle of the arm. Blood pressure was 95/60 in both arms and 105/60 in the leg. No ocular pathology was reported by the ophthalmology consultant.

She was examined by Dr. Ralph C. Benson, the gynecologic consultant, who reported that there was only minimal development of the cervix uteri. The right ovary could not be felt, but there was some question of an ovarian vestige on the left.

Roentgenograms for bone age showed that it was equal to the chronological age. No osteoporosis was present, and no roentgen evidence of any abnormality was noted in the chest, spine, skull, or extremities.

On May 27, 1951, a 24-hour urine specimen was positive at 5 mouse units for gonadotropins and negative at 80 mouse units. On June 14, 1951, it was positive at 30 mouse units for gonadotropins and negative at 5 mouse units. A 24-hour urine specimen was negative for estrogenic hormone. On June 25th and 26th, assays were made in two different laboratories, and both were positive at 5 mouse units and negative at 50 mouse units. There were 1.2 mg. of 17-ketosteroids in a 24-hour urine specimen.

The reaction to the Kolmer and Kahn tests was negative.

Examination of the stools for parasites revealed ova of Trichuris trichiura on one occasion.

Blood serum calcium was 10.6 mg. per 100 cc., phosphorus 4.6 mg. per 100 cc., basic phosphatase 9 units, and total protein 6.8 gm. per 100 cc. The blood examination revealed hemoglobin 13 gm. per 100 cc.; red blood cell count 3,800,000, and white blood cell count 6,650, with 46% neutrophiles, 45% lymphocytes, 2% monocytes, and 7% eosinophiles.

CASE 3 (previously reported).—J. L. was born at term following a normal delivery and weighed 5 lbs. 8 oz. (2,495 gm.). A large fold of extra skin which had formed a web on the neck posteriorly had been noted at birth. The feet also were malformed. The child had excellent health with a good appetite and received a well-balanced diet. Adequate amounts of supplemental vitamins were given, and her first tooth had erupted at the age of 6 months.

Both parents and a younger sibling were of normal height. At 2½ years of age, a plastic operation was performed on the webbed neck, and the question of Turner's syndrome ("infantilism, congenital webbed neck, and cubitus valgus") arose. Physical examination revealed a persistence of the deformity of the feet, and there was a questionable increase of the carrying angle of the arm (cubitus valgus). No abnormality of the heart was noted. The first urinary

gonadotropin assay was found to be positive at 15 mouse units per 24 hours. Three out of five subsequent assays of urinary gonadotropins were positive at 5 mouse units, but all were negative at 8 units. Roentgenograms of the skull demonstrated no disease, but those of the spine showed changes which were considered to be typical of those found in juvenile epiphysitis. An error in development of the lumbar vertebrae was present. The bone age was slightly retarded. At exploratory laparotomy a rudimentary uterus and elongated whitish ovarian streaks were found. Microscopic examination of the biopsy material showed it to be characteristic of ovarian agenesis. No primordial ova were seen.

COMMENT

From a review of the literature, the most frequently described anatomic, biologic, and clinical manifestations of the syndrome of ovarian agenesis have been as follows:

A. Manifestations present before puberty
   1. Shortness of stature of moderate degree in most, but not all, cases
   2. Good muscular development, the patients being strong and well-nourished and with a broad shield-like chest
   3. Congenital anomalies, such as webbing of the neck, cubitus valgus, syndactylism, coarctation of the aorta, and ocular changes
   4. Rudimentary ovarian development
   5. Increased urinary gonadotropins
   6. Moderate retardation of skeletal maturation with delay in epiphyseal closure

B. Manifestations evident after puberty
   1. Subnormal titers of urinary estrogens
   2. Diminished 17-ketosteroids of the urine
   3. Diffuse osteoporosis
   4. Primary amenorrhea
   5. A decrease, but not total absence, of axillary and pubic hair
   6. Infantile breasts, uterus, vagina, and labia

The only findings that our three prepubertal patients had in common on physical and laboratory examination were as follows:

1. Shortness of stature
2. Good nutrition and muscular development
3. A broad shield-like chest with widely spaced nipples
4. Abnormally small uterus
5. Increased urinary gonadotropins

Shortness of stature is a common but not constant finding in this syndrome. Shortness of stature was only of moderate degree, and, as far as could be ascertained, growth had been occurring at a normal rate in two of the three children. It would thus appear that in these children the expected relative marked degree of dwarfing that becomes apparent in adult life will be due to a failure to have the normal pubertal spurt. If the growth of these patients is projected on to adult life, it is found that they would reach heights of approximately 55 in. (140 cm.), which is the approximate height that most patients in the reported cases[8] have reached. However, in certain reported cases growth always was at a subnormal rate.

8. Goldberg, M. B.; Maxwell, A. F., and Smith, P. M.: Three Unusual Endocrinopathies with Associated Ovarian Pathology: I. Ovarian Agenesis. II. Precocious Puberty. III. Virilism, J. Clin. Endocrinol. **7**:11, 1947.

All three individuals were stockily built and had good musculature, but had the appearance of normal children somewhat younger than their chronological ages. In two cases the wide spacing of the nipples, producing a "shield-shaped chest" (Lisser and associates) [9] in children with shortness of stature, was the initial clue which led us to obtain assays of urinary gonadotropins and to proceed with other studies which aided in making the diagnosis.

Various congenital abnormalities have been described in this syndrome, including cubitus valgus (increased carrying angle of the arm), congenital webbed neck, pes cavus at rest, congenital deafness, coarctation of the aorta, and various ocular abnormalities (squint, ptosis, cataracts, tubular vision, mild exophthalmos, and lack of retinal pigmentation). Of these cubitus valgus and the congenital webbed neck are the two present most often in this syndrome. Webbed neck was found in only one of our patients, but two of them had some congenital defect of the feet.

Biopsy of the ovary was carried out in only one child. The result of the examination of ovarian tissue in that patient demonstrated the fact that the finding of elevated urinary gonadotropins could be used to establish the diagnosis of ovarian agenesis in prepubertal girls. We did not feel that sufficient information of a practical nature could be obtained from ovarian biopsies in the other cases to make the procedure necessary, since all of our other data seemed so clear-cut. In all three patients the gynecologic consultant reported that the uteri were much smaller than normal for the age and would have been unusually small even for a newborn child.

Osteoporosis was noted only in the older child (aged 12 years 5 months), although it has been a relatively common finding in the older females. Van Creveld and De Vaal noted it in a 14-year-old child, but in general it has not been described in the reports of the younger children, and it would appear to be a late finding which would be of minor diagnostic help early in life.

We now consider the diagnosis of ovarian agenesis in every child with shortness of stature in whom no obvious cause for the dwarfing can be determined. We believe that this is necessary since there are no pathognomonic signs or symptoms of the syndrome, and only by the demonstration of levels of urinary gonadotropins elevated for the age can the diagnosis be made.

In his excellent textbook, Wilkins reports: "The youngest patient with ovarian agenesis in whom we have found a titer of FSH above the normal adult level was 12 years old," and he suggests: "An elevation of the FSH will not be found before the age of 10 to 12 years when the secretion of pituitary gonadotropin first begins." However, in at least two of our patients, the elevated excretion of gonadotropins was found long before the expected time for puberty.

An increase in urinary gonadotropins is the most important single clinical or laboratory finding in making the diagnosis of ovarian agenesis. However, it should be emphasized that in our two younger patients the excretion of gonadotropins in the urine would not have been abnormally high for an adult but was higher than that found in the normal prepubertal female. The oldest child, at an age when most

9. Lisser, H.; Curtis, L. E.; Escamilla, R. F., and Goldberg, M. B.: Syndrome of Congenitally Aplastic Ovaries with Sexual Infantilism, High Urinary Gonadotropins, Short Stature and Other Congenital Abnormalities: Tabular Presentation of 25 Previously Unpublished Cases, J. Clin. Endocrinol. **7**:665, 1947.

girls are in the early phases of puberty, excreted more than 160 mouse units of gonadotropins per day, a level not found for any normal women during the reproductive period.

Albright and associates [10] have suggested that the mechanism for the production of excessive amounts of urinary gonadotropins is an "unbridling" of the hypophysis when there is an absence of effect of ovarian hormones with the resultant production of an exaggerated quantity of these substances. This "unbridling" apparently may occur even in childhood (as evidenced by the excretion of abnormally large amounts of gonadotropins), and this suggests that the preadolescent ovary may produce small amounts of estrogens or other substances which keep the hypophysis in check.

A delay in the bone age in relation to the chronologic age has been described in many patients. Although there was some retardation in two of our patients, it was not severe and was no more marked in the 12-year-old patient than in the child who was only 2 years 8 months old. Thus, it would appear that the delay becomes more evident after the normal age of puberty.

After reviewing the clinical, laboratory, and pathologic findings in the reported cases, as well as our own, it appears that no single physical finding is present in every instance. Although primary amenorrhea and signs of sexual infantilism are prominent in the adult cases, they are not indispensible parts of the syndrome, and it is possible to make the diagnosis at a time of life when such findings are entirely normal.

Differentiation of ovarian agenesis from other diseases which disturb growth or modify the development of the sexual organs may be difficult. Primary pituitary infantilism is the most important condition to be considered, since it is also characterized by shortness of stature and retarded sexual development. The outstanding differential point is the urinary excretion of pituitary gonadotropins, which is absent in pituitary infantilism as contrasted with the decidedly high titers found in ovarian aplasia. The older patients suffering from ovarian aplasia are as a rule not as tiny as pituitary dwarfs; they have more pubic and axillary hair than the latter and are well nourished, with a stocky build and a broad deep "shield chest" in contradistinction to the slender gracile Levi-Lorain type of skeleton typical of hypophyseal infantilism. The bone age is only slightly retarded in ovarian aplasia in contrast to the much greater retardation of pituitary dwarfism. The presence of other congenital anomalies, such as coarctation of the aorta, webbed neck, and cubitus valgus, also may aid in making the correct diagnosis, since they usually have not been observed in association with primary pituitary infantilism.

Hypogonadism due to removal or ablation of the gonads is more easily diagnosed when it originates in childhood, since females with this disorder tend to be tall and typically have disproportionately long extremities. The rate of the follicle-stimulating hormone excretion does not help to differentiate this condition from ovarian aplasia, since it is high in both.

Hypothyroidism, mongolism, severe malnutrition, childhood diabetes, renal rickets, or congenital heart disease are other causes of dwarfing; a differential diagnosis may be readily made by the clinical picture and the performance of the proper diagnostic tests.

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10. Albright, F.; Smith, P. H., and Fraser, R.: Syndrome Characterized by Primary Ovarian Insufficiency and Decreased Stature: Report of 11 Cases with Digression on Hormonal Control of Axillary and Pubic Hair, Am. J. M. Sc. **204**:625, 1942.

The association of shortness of stature with genital impairment and high urinary gonadotropins in ovarian agenesis has not been explained satisfactorily. Albright has offered the hypothesis that the decrease in estrogenic substance production leads to a secondary change in the adrenal cortex which, in turn, results in a decreased growth rate. Wilkins and Fleischmann [11] point out that if the stunting of growth were due to diminish adrenal activity in patients with ovarian agenesis, one would expect them to grow normally through the preadolescent period but to fail making an adolescent growth spurt. Many of the reported case histories do not indicate that this is so, but in two of our patients, as well as in some others, such a pattern of growth did occur. Most authors explain the occurrence in one syndrome of congenital anomalies involving such diverse structures as the gonads, skeleton, cardiovascular system, and eyes on a genetic basis and are of the opinion that the deficient growth is due to a defect in the germ plasm rather than to an endocrine disturbance.

SUMMARY

Three cases of ovarian agenesis in girls aged 2 years 8 months, 8 years 10 months, and 12 years 5 months, respectively, are presented.

All three patients were short of stature and had good nutrition and muscular development, broad shield-like chests with widely spaced nipples, abnormally small uteri, and increased excretion of urinary gonadotropins.

Department of Pediatrics, Yale University School of Medicine (Dr. Silver).

11. Wilkins, L., and Fleischmann, W.: Ovarian Agenesis: Pathology, Associated Clinical Symptoms and Bearing on Theories of Sex Differentiation, J. Clin. Endocrinol. **4**:357, 1944.

CYSTINOSIS

Report of Two Cases with Postmortem Examination

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THE FIRST case of cystinosis was recorded by Abderhalden and Kaufmann in 1903.[1] No other cases were reported until 1924, when Lignac reported two, and in 1925, when he added another.[2] Some writers refer to the condition as Lignac's disease. Ten years later, in 1935, Benoit's case was published,[3] and since that time there were 13 more, which makes a total of 18. None of these were in America.

TABLE 1.—*Published Cases of Cystinosis with Autopsy*

Year	Author	No. Cases	Place	Sex	Age, Yr.
1903	Abderhalden and Kaufmann [1]	1	Berlin	M	1 9/12
1924	Lignac [2]	2	Leyden	M	3
				M	2
1925	.....	1	.....	F	1 3/12
1935	Benoit [3]	1	Jena	M	3 1/12
1937	Beumer [4b]	1	Göttingen	M	1 9/12
1938	Rössle [4c]	1	Berlin	F	4
1940	Pache [4d]	1	Marburg	M	7 9/12
1941	Hottinger [4e]	1	Basel	M	7 9/12
1946	Fanconi [4f]	2	Zürich	F	7
				F	3 11/12
1946	Russell and Barrie [4g]	2	London	M	12
				F	16
1947	Hottinger [4h]	1	Basel	M	11
1950	Jackson and Clarke	2	New York	M	7 5/12
				F	7 5/12
	Total	16			

From the Departments of Pediatrics and Pathology, St. Luke's Hospital.

Presented before the Friday Night Medical Club, Providence, R. I., March 23, 1950.

Pathologic aspects presented at the 47th Annual Meeting of the American Association of Pathologists and Bacteriologists, Madison, Wis., April 15, 1950.

1. Abderhalden, E.: Familäre Cystindiathese, Ztschr. physiol. Chem. **38**:557, 1903.

2. Lignac, G. O. E.: Über Störung des Cystinstoffwechsels, München. med. Wchnschr. **71**:1016, 1924; Stoornis der cystine stoff-wisseling bij kinderen in verband mit dierproven, Nederl. tijdschr. geneesk. **68**:2987, 1924; **69**:819, 1925; Nephrose en nephritis door cystine, ibid. **69**:611, 1935.

3. Benoit, W.: Calcinosis universalis, Beitr. path. Anat. **94**:611, 1935.

Fourteen of the 18 cases came to postmortem examination. Our two are the 15th and 16th cases with postmortem examinations and the first to be reported in the United States (Table 1).[4]

REPORT OF CASES

CASE 1.—Jacqueline M. was first admitted to St. Luke's Hospital on Aug. 24, 1942, at the age of 3½ years. The admission history as obtained from the mother is related with some detail because it is thought to be characteristic.

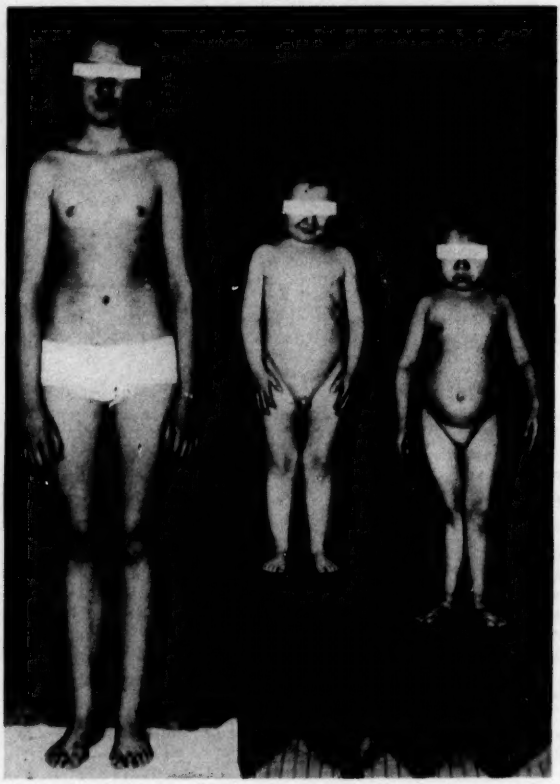

Fig. 1.—Photograph of the three siblings taken April 3, 1946. The normal sister (left), age 14 years, John (center), age 5 years 9 months, and Jacqueline (right), age 7 years 3 months. The dystrophy is obvious in Jacqueline. John, at this time, was much better nourished than at time of admission in 1942 (see Fig. 2).

4. (*a*) Footnotes 1, 2, and 3. (*b*) Beumer, H., and Wepler, W.: Über die Cystinkrankeit der Ersten Lebenszeit, Klin Wchnschr. **16**:8, 1937. (*c*) Rössle, R.: Beiträge zur Frage der Speicherungskrankheiten, Verhandl. Gesellsch. Verdauungskr. (1938) **14**:133, 1939. (*d*) Pache, H. D.: Über die Cystein-Cystin-Stoffwechselstörung der ersten Lebenszeit und ihre Beziehung zu Zwergwuchs und renaler Rachitis, Ztschr. Kinderh. **62**:1, 1940. (*e*) Hottinger, A.: Über Cystindiathese, Ann. pædiat. **156**:257, 1941. (*f*) Fanconi, G.: Weitere Beiträge zur Cystinkrankheit (der Aminodiabetes), Helvet. paediat. acta **1**:183, 1946. (*g*) Russell, D. S., and Barrie, H. J.: Storage of Cystine in the Reticulo-Endothelial System and Its Association with Chronic Nephritis and Renal Rickets, Lancet **2**:899, 1936. (*h*) Hottinger, A.: Zur Cystindiathese, Ann. pædiat. **169**:272, 1947.

She was born after a normal full-term pregnancy, with spontaneous delivery following a 25-minute labor. There was no evidence of birth injury or respiratory distress. At birth her weight was 7 lb. 1 oz. (3,100 gm.) and her length 19 in. (48 cm.). After only 12 days of breast feeding, she was placed on a formula of whole cow's milk (unboiled) and Dextri-Maltose. Vitamin D and orange juice were given in adequate amounts throughout life. Cereals were started in the third month, egg yolk in the fourth month, and vegetables in the fifth month. During this period there was a steady weight gain of 4 to 6 oz. (114 to 170 gm.) per week. At 6 months of age she weighed 14 lb. 15 oz. (6,775 gm.). At about this time the baby became severely constipated. With magnesia magma U. S. P. (milk of magnesia) given directly in the formula every day, the constipation improved somewhat, but she began to lose weight.

There followed a period of changing doctors, when various formulas and medications were tried, including theyroid, acidophilus milk, a calcium caseinate preparation (Casec), and cascara sagrada. She remained listless and did not gain weight. At 11 months she weighed 14 lb. (6,350 gm.). About this time it was noticed that the child "liked water" and drank large quantities of it. There was marked nocturia. She also had a great appetite for salt and took her food much better if allowed to shake the salt on it herself. At the age of 1 year and 8 months, her weight was 15 lb. 4 oz. (6,920 gm.), but this fell to 12 lb. 11 oz. (5,750 gm.) at 2 years. At 2 years and 8 months her weight was 15 lb. (6,800 gm.), and at time of admission, 3 years and 7 months, 18 lb. 8 oz. (8,400 gm.).

The abdomen became quite distended after the age of 1 year and 8 months. She wore a "basilar" belt for this. The stools were never greasy, foamy, or bloody. During the last year there were attacks of vomiting after feeding. The mother related this to the addition of egg to the diet.

The child held her head up at 3 months and had her first tooth at 6 months. She spoke at 11 months and sat up at 11 months. She did not crawl, but pushed herself about in a "walker" at 1½ years. She stood alone at 3 years, but did not walk. In spite of long-standing nutritional difficulty, she was free from colds and other infections, except for measles, when 3 years old.

Physical Examination.—When Jacqueline was first examined, on Aug. 18, 1942, she presented a striking appearance. Her facies was Mongoloid, the hair sparse and unruly, and the skin dry and very yellow. There was marked "knock-knee" that interfered with her walking. Because of the long duration of her illness and her failure to gain, she appeared dwarf-like beside the other, older sibling (Fig 1).

In spite of her appearance and of the many manifestations of severe dystrophy, her mentality was unimpaired until the latter months of her life. She was readmitted nine times. The important findings of the hospital studies are shown in Table 2. She died in the hospital at the age of 7 years and 8 months.

Case 2.—Jacqueline's brother, John M., was first admitted one month later than his sister, on Sept. 24, 1942, at the age of 15 months.

The history of John's first 15 months was almost identical with his sister's. At birth his weight was 8 lb. 2 oz. (3,700 gm.) and his length, 21 in. (53 cm.). He was considered a normal healthy baby until about the fifth month, after which he was constipated and failed to gain and develop properly. He was admitted at an earlier age than his sister and therefore studied longer and more completely.

Physical Examination.—At the time of first admission, he weighed 16 lb. 4 oz. (7,370 gm.) and measured 29 in. (74 cm.) in height. He was described as being poorly nourished and as having a flabby musculature. The anterior fontanelle admitted one finger, and there was marked craniotabes and frontal and parietal bossing. There was a marked rachitic rosary with a deep Harrison groove (Fig. 2). The heart and chest were considered normal. The abdomen was soft, with the liver edge palpable at the costal margin. The spleen was not felt. The extremities showed enlarged radial epiphyses and the beginning of bowed legs.

Laboratory data and other important findings of this and subsequent admissions are shown in Table 3.

TABLE 2.—*Findings on Hospital Studies*

Hosp. Adm.	Age, Yr.	Ht., In.	Wt., Lb.	Urine			Hemogram			
				Sp. Gr.	Alb.	Microscopic Findings	Hgb., Mg./ 100 Cc.	Red Blood Cells	White Blood Cells	Diff. Count
(1) 9/-/42	3 7/12	31¼	18½	.....	2+	1-4 WBC	12.1	4,300,000	14,500	Normal
(2) 4/-/43	4 3/12	34¾	22	.....	2+	1-5 WBC; occasional RBC; occasional granular casts	11.6	3,940,000	19,900	Shift to left
(3) 1/-/44	4 11/12	....	20	.....	1+	1-5 WBC; rare RBC	11.4	4,100,000	15,700	Slight shift to left
(4) 4/-/45	6 3/12	34¼	24	1.005	1+	Few WBC	6.1	2,100,000	15,400	Normal
(5) 9/-/45	6 7/12	35½	23½	.....	...	.....	7.3	2,700,000	21,000	Normal
(6) 9/-/45	6 7/12	....	23	1.008	1+	Occasional WBC; few granular casts	11.0	3,900,000	20,200	Shift to left
(7) 4/-/46	7 3/12	35	27	1.010	1+	Occasional WBC	6.7	2,100,000	15,900	Normal
(8) 6/-/46	7 5/12	36	30	.....	...	.....	7.9	2,400,000	8,500	Slight shift to left
(9) 8/-/46	7 7/12	35½	25½	.....	2+	Occasional WBC	3.0	750,000	6,700	Normal
(10) 9/-/46	7 5/12	35	28	.....	1+	.....	7.8	2,680,000	10,700	Normal

TABLE 3.—*Findings on Hospital Studies*

Hosp. Adm.	Age, Yr.	Ht., In.	Wt., Lb.	Urine			Hemogram			
				Sp. Gr.	Alb.	Microscopic Findings	Hgb., Mg./ 100 Cc.	Red Blood Cells	White Blood Cells	Diff. Count
(1) 9/-/42	1 3/12	29	16¼	1.016	3+	1-4 WBC; 1-2 RBC; no cystine crystals	9.3	3,750,000	8,800	Shift to left
(2) 4/-/43	1 10/12	30	18¼	1.010	3+	Few WBC; occasional hyaline casts	10.5	3,820,000	14,700	Shift to left
(3) 6/-/45	3 11/12	....	23	1.004	1+	Normal	11.8	4,100,000	10,850	Normal
(4) 4/-/46	4 10/12	34	25	1.010	Negative	Normal	14.6	5,400,000	5,700	Slight shift to left
(5) 11/-/46	5 5/12	36	25	1.010	3+	Occasional WBC	11.6	4,150,000	14,450	Normal
(6) 12/-/46	5 6/12	36½	27½	.....	3+	30-40 WBC; few pus clumps	...	.....	.....	.....
(7) 2/-/47	5 5/12	36½	29½	1.010	3+	Few WBC; many granular casts	9.2	3,900,000	13,300	Normal
(8) 5/-/47	5 11/12	36½	30	.....	3+	Rare WBC and RBC; occasional hyaline casts	9.8	3,100,000	10,000	Slight shift to left
(9) 10/-/47	6 3/12	37½	31½	1.001	2+	3-5 WBC; 7-10 RBC; hyaline and granular casts	8.2	2,400,000	6,800	Normal
(10) 11/-/47	6 5/12	37	31½	.....	2+	Rare WBC	7.3	2,380,000	7,300	Normal
(11) 2/-/48	6 8/12	37	30	1.009	2+	Rare WBC	7.9	2,610,000	8,400	Normal
(12) 3/-/48	6 9/12	37¼	30	1.014	3+	Occasional WBC; rare RBC; rare hyaline casts	8.8	2,550,000	6,400	Normal
(13) 5/-/48	6 11/12	37¾	31¼	1.009	3+	Normal	9.4	3,330,000	10,900	Normal
(14) 6/-/48	7	38	31¾	1.010	3+	Normal	7.4	2,140,000	5,200	Normal
(15) 8/-/48	7 3/12	39	33½	1.010	1+	Occasional WBC	...	.....	.....	.....
(16) 8/-/48	7 3/12	39	37½	1.010	3+	Occasional WBC; rare granular casts	8.8	3,440,000	7,700	Normal
(17) 9/-/48	7 3/12	....	37	1.013	4+	Occasional WBC	9.2	3,020,000	5,400	Normal

of Jacqueline M., Born Jan. 28, 1939

Chemistry											X-Ray		
Urea N, Mg./ 100 Cc.	NPN, Mg./ 100 Cc.	CO_2, Vol. %	Ca, Mg./ 100 Cc.	P, Mg./ 100 Cc.	Alk. Phos., Mg./ 100 Cc.	Chol., Mg./ 100 Cc.	Sugar, Mg./ 100 Cc.	PSP,	ECG	B. P.	Chest	Pyelogram	Long Bones
31.5	..	31.5	13.2	3.6	6.2	308	100	27%	..	80/40	..	Moderate dilation; renal pelves, calyces normal, ureters tortuous	Uniform decalcification changes of rickets
27.9	..	40	12.6	4.3	4.5	272	...	..	..	.....	Normal	.....	Recession of rachitic changes
....	..	..	8.8	4.7	8.3	...	...	..	..	.....	..	Small area of constriction at ureteropelvic junctions	No irregularity of epiphyseal line as seen previously; epiphyses stippled
....	144	20	7.0	8.9	14.9	...	90	1%	..	90/40	..	.....	.....
65	84	..	8	6.7	23.7	...	...	..	..	95/40	..	.....	.....
....	92	21	5.3	...	...	...	...	..	..	70/0	..	.....	.....
150	163	16	7.5	6.3	22.9	...	...	..	..	80/40	..	.....	.....
....	..	..	7.0	...	...	...	...	..	..	.....	..	.....	.....
22.8	89.9	23	6.5	6.2	...	308	...	..	..	.....	..	.....	.....
127	145	13.5	4.4	9.7	7.3	...	...	..	Normal	112/98	Normal	.....	.....

of John M., Born June 27, 1941

Chemistry											X-Ray		
Urea N, Mg./ 100 Cc.	NPN, Mg./ 100 Cc.	CO_2, Vol. %	Ca, Mg./ 100 Cc.	P, Mg./ 100 Cc.	Alk. Phos., Mg./ 100 Cc.	Chol., Mg./ 100 Cc.	Sugar, Mg./ 100 Cc.	PSP,	ECG	B. P.	Chest	Pyelogram	Long Bones
125	31.3	..	13	2.9	6.7	267	...	19%	..	.....	..	Renal pelves slightly enlarged; ureters normal	Marked cupping and irregularity of ends due to rickets
24	..	30	12	4.3	5.3	238	...	..	..	.....	..	.....	.....
....	53.7	..	10.8	4.3	...	...	...	..	..	.....	..	.....	.....
36	61	46	9.8	5.5	10.3	...	...	..	..	75/40	Normal	.....	Same pathology with some improvement
31.6	..	33	8.5	6.2	14.6	414	...	..	..	.....	..	.....	.....
....	..	..	....	...	...	...	...	..	..	.....	..	Slight constriction of ureters	.....
40	..	70	8.3	...	...	...	...	..	..	.....	..	.....	.....
....	..	..	....	...	...	...	...	..	..	.....	..	Slight dilatation of ureters; renal pelves and calyces normal	.....
22.2	48	22	7.6	...	...	...	...	..	..	.....	..	.....	.....
....	..	..	....	...	...	...	...	..	..	.....	..	.....	.....
40.9	..	31.7	7.8	6.1	16.5	...	...	..	..	98/55	..	.....	.....
76.8	..	30.5	7.4	6.9	16.5	...	67	..	Normal right axis deviation	.....	Lungs clear; heart upper limit of normal	.....	Progression in bone changes; further irregularity in epiphyses
83.2	..	43	9.3	6.7	6.6	...	...	..	..	.....	..	.....	.....
76.4	..	..	9.6	7.4	5.2	...	...	..	..	.....	..	.....	.....
112.4	..	39	10.1	9.1	4.3	...	...	Trace	Normal rhythm	.....	..	.....	.....
104.2	..	43.9	....	...	...	...	...	..	..	100/50	Normal	.....	Definite improvement; less irregularity of epiphyseal-metaphyseal line; increase in bone density
142.8	..	37.4	11.1	12.0	7.2	...	...	..	..	135/80	..	.....	.....

Calciferol (Drisdol) therapy was started, and on admissions at the age of 2, 4, and 5 years the roentgenograms were reported to show progressive improvement of osseous development. During the sixth year, there were several episodes of carpopedal spasm. This was treated with ascorbic acid. Bed wetting persisted. Because pyelograms showed slight constriction of the ureters, dilation was done on two occasions. At the ninth admission, in Sept., 1947, it was clinically evident that he was in acidosis. The liver and spleen were both

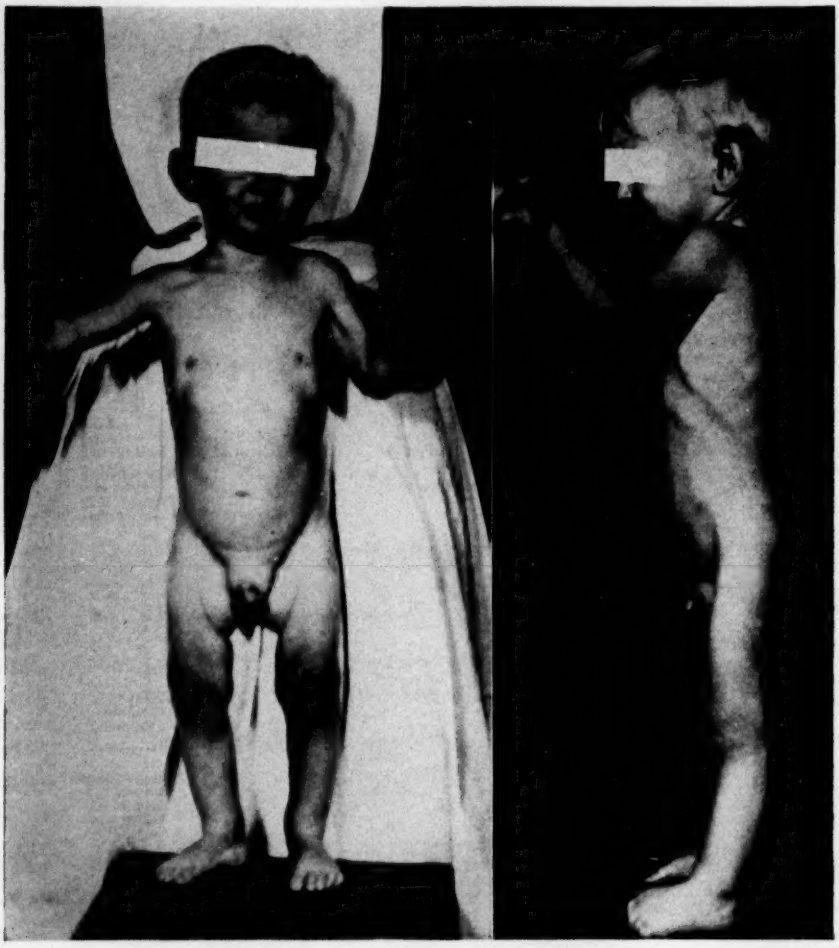

Fig. 2.—John at time of admission (Oct. 5, 1942). The flabbiness, rachitic rosary, and Harrison's groove are well shown.

enlarged. He responded to therapy with lactated Ringer's solution and calcium gluconate. Following this he was admitted several times for tetany and three times for blood transfusions. Table 3 is a review of all of these admissions.

John's 17th and final admission, on Aug. 27, 1948, was preceded by a five-day period of lethargy, headache, and vomiting. On the day of admission he had a convulsion and became comatose. The blood urea nitrogen was 142.8 mg. per 100 cc. The liver and spleen were palpable. After intravenous administration of fluids, the blood urea nitrogen fell to 51 mg.

per 100 cc., and he seemed clinically improved. There was evidence of easy bleeding with tarry stools and epistaxis. During the second week, an abscess which developed on the anterior chest wall was drained. The blood urea gradually increased, and during the third week the blood pressure became elevated to 180/110. Frank edema developed, and convulsive seizures became more frequent, necessitating sedation. He became disoriented, lapsed into a coma, and died on the 25th hospital day.

The clinical opinion was that these two children had a congenital anomaly of the urinary tract with resulting renal failure, secondary hyperplasia of the parathyroid glands, renal rickets, cardiac failure, and terminal uremia.

In John, the much earlier admission and resulting care and treatment postponed the typical signs of renal rickets until the latter months of his life; yet the pattern of the disease was not changed in any way, and the end result was the same.

PATHOLOGY

The postmortem findings in the two cases were almost identical. Each child was markedly underveloped and poorly nourished. Jacqueline's body measured 35½ in. (90 cm.) in length and weighed 25 lb. (11,340 gm.). That of John measured 39½ in. (98 cm.) and weighed 36 lb. (16,330 gm.). Both children were 7 years old at the time of death.

The heart in each case weighed 175 gm. (normal for a height of 97 cm. is 73 gm.), and the girl had a fibrinous pericarditis (uremic). John's liver weighed 925 gm. (normal, 516 gm.) and tiny irregular yellow-white spots were scattered through it. The weight of John's spleen was 160 gm. and of Jacqueline's, 275 gm. (normal 39 gm.). Tiny yellow-white spots were visible in John's spleen. His parathyroid glands were hypertrophied (2 by 3 by 7 mm.). Jacqueline's were not examined. In John, the mesenteric lymph nodes were large and had a peculiar yellowish-brown color. John's kidneys each weighed 25 gm. (normal 57 gm.). Jacqueline's were not weighed, but measured only 5 by 3 cm. The capsules stripped with difficulty from a pale finely nodular surface. The cortices were irregularly thinned, pale, and devoid of normal markings. The pelves, ureters, bladders, and urethras were not remarkable.

The microscopic findings were quite unexpected. Collections of crystalline material were deposited in the tissues. Much of this material was in the form of tiny irregular fragments, but some large hexagonal crystals and some rectangular crystals were present. Many were rounded suggesting hexagons with damaged edges. This material was found to be soluble in hydrochloric acid and in ammonia. Chemical tests for cystine were positive.

The cystine was most abundant in the spleen. It was deposited in the splenic pulp and in the splenic corpuscles and was seen in phagocytic cells within the sinuses. It was both free in the tissues and within mononuclear phagocytes. There was increased fibrous tissue and an infiltration of eosinophiles. Much of the enlargement of the spleen was due to chronic passive congestion (Fig. 3).

The lymph nodes also contained a great deal of cystine. It was most abundant in the cortex, both within the germinal centers and within the intervening tissue. Again, it was both free in the tissues and within phagocytes. There was no fibrosis, but there were numerous eosinophiles (Fig. 4).

In the liver, the larger deposits of cystine were within the portal spaces, but the Kupffer cells were frequently distended with it, and it was sometimes seen within liver cells (Fig. 5*A*). In the case of John, there were areas of focal necrosis in the liver not associated with cystine.

Jacqueline's thyroid was not examined, but cystine was abundant in John's. The acini were frequently filled with large mononuclear cells distended with it. It was also seen within the epithelial cells lining the acini. This suggested that the cells filling the acinar lumina were desquamated epithelial cells. The cystine was also abundant in the stromal tissue of the thyroid (Fig. 5*B*).

Cystine was also found in the intestinal mucosa, in the lungs, in the adrenal glands, in the pancreas, and in the testicles. None was found in the heart or in the musculature of the gastrointestinal tract. Voluntary muscle was not examined. No cystine was found in the central nervous systems.

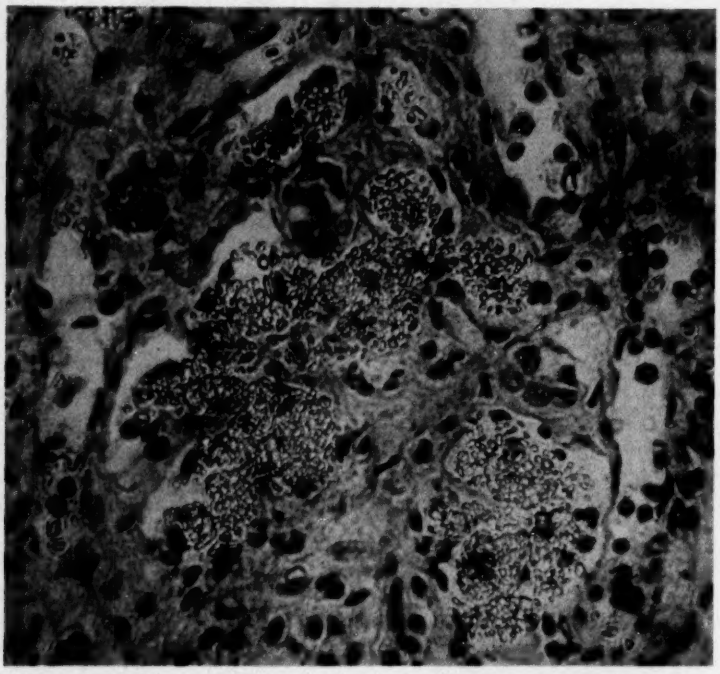

Fig. 3.—Photomicrograph of spleen. Large mononuclear phagocytes having cytoplasm packed and distended by the cystine crystals are numerous. Some of the cystine is free in the tissues. Hematoxylin and eosin stain. The chronic passive congestion is evidenced by the dilated sinuses.

The presence of cystine in the parenchymatous cells of the liver and in the epithelial cells of the thyroid gland is apparently unusual. Other reports describe it only in the interstitial tissues and in the phagocytic cells.

In the kidneys, cystine deposit was not conspicuous. Most of that seen was deposited in the stroma, some free and some within phagocytic cells (Fig. 6*A*). The kidneys were badly damaged. No normal glomeruli remained.

In the girl's kidneys, most glomeruli showed the vascular tuft reduced to a small hyaline mass. About it the capsule was frequently thickened and hyalinized (Fig. 6*B*). In the boy, the same atrophy and hyalinization was found, but, in addition, many of the glomeruli showed proliferative changes like those seen in

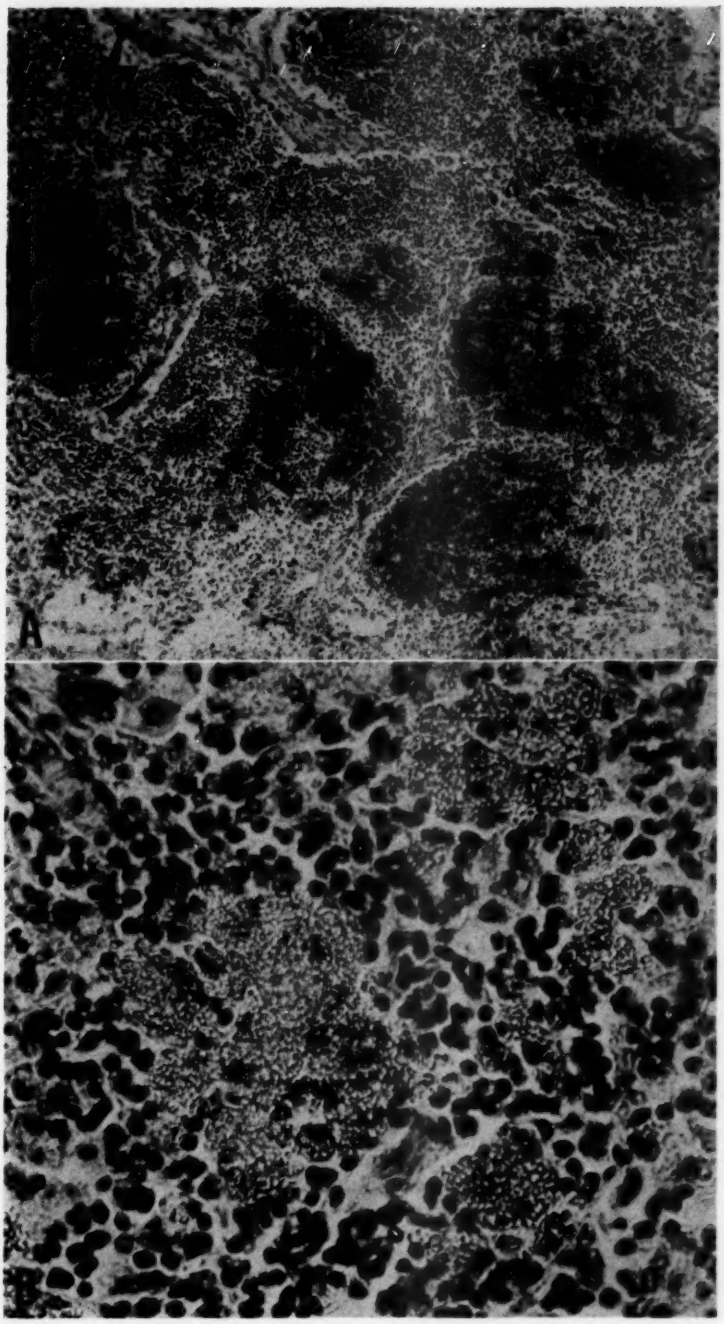

Fig. 4.—*A*, low-power photomicrograph of lymph node showing the great abundance of cystine appearing as irregular dark granular areas. *B*, high-power photomicrograph of lymph node shows the cystine crystals within phagocytes and free in the tissues. Hematoxylin and eosin stain.

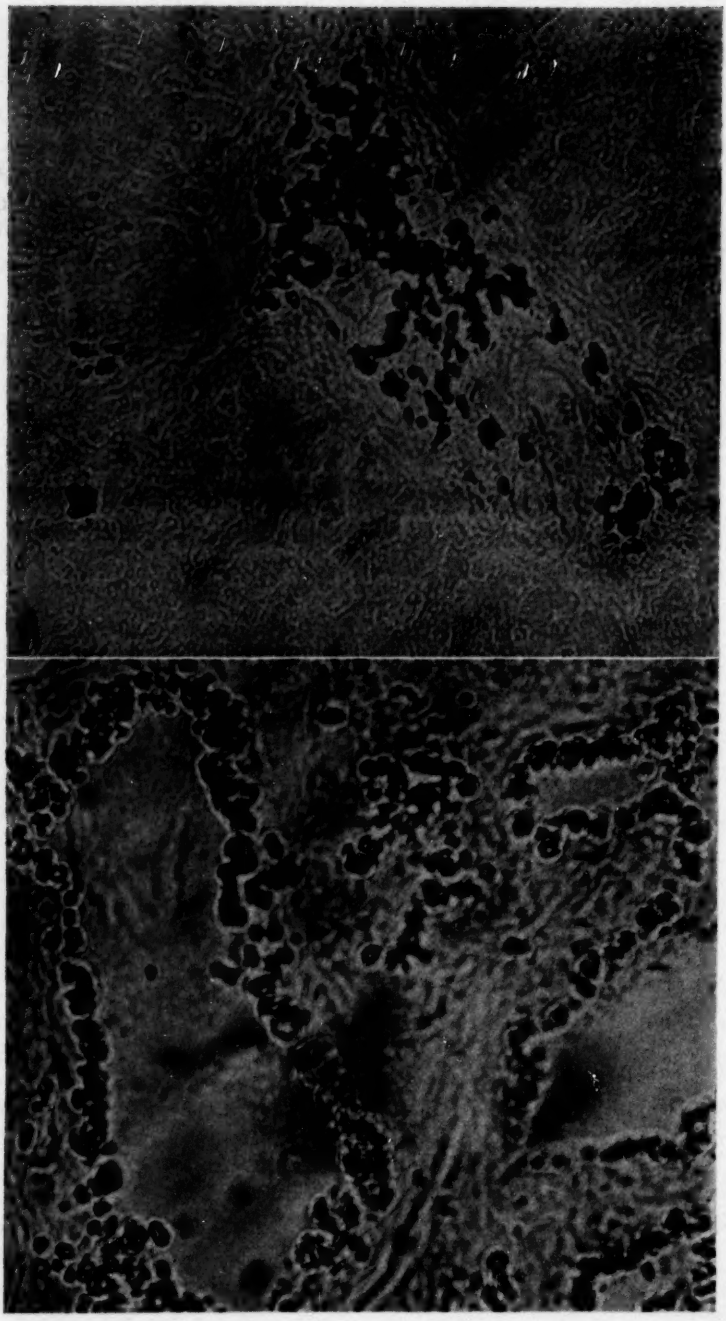

Fig. 5.—*A*, photomicrograph of liver showing cystine in the portal space (upper central) and within Kupffer's cells (lower). Unstained paraffin section. *B*, photomicrograph of thyroid gland showing the cystine within the cytoplasm of the epithelial cells lining the thyroid acini. Unstained paraffin section.

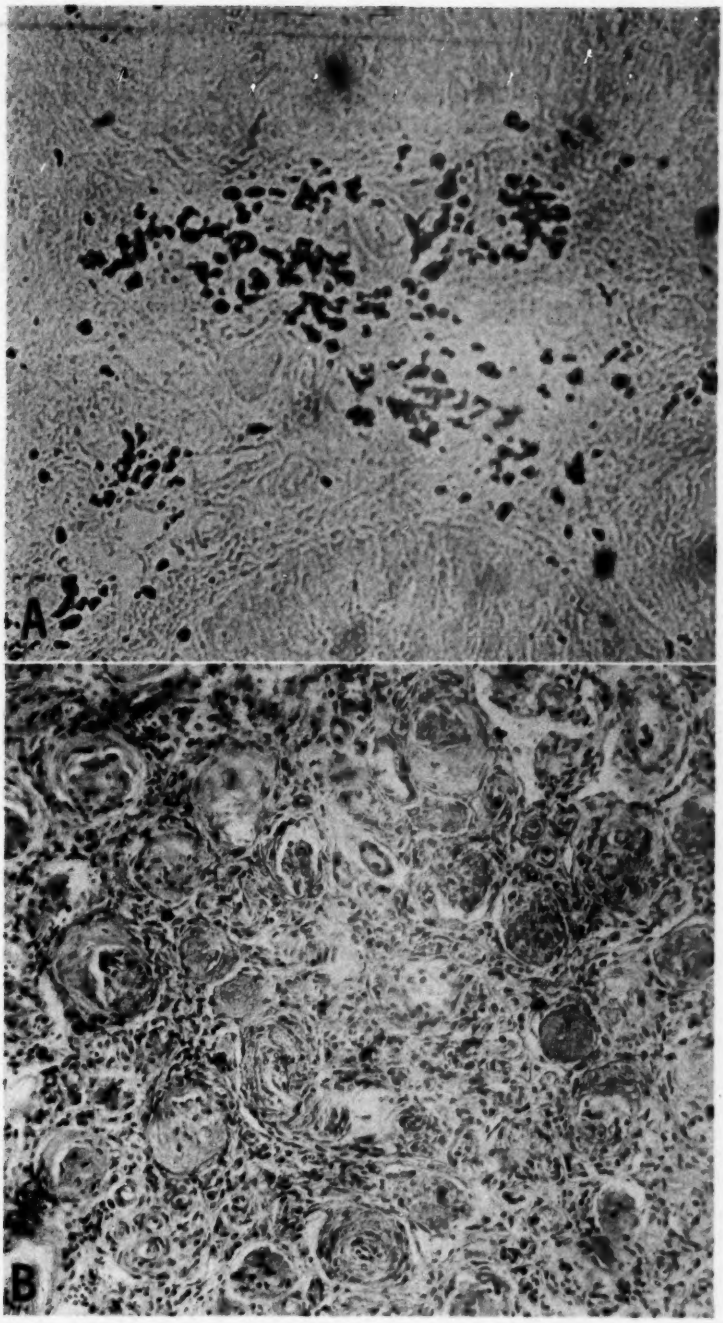

Fig. 6.—*A*, photomicrograph of unstained paraffin section of kidney showing cystine within phagocytic cells and free in the increased fibrous stroma. *B*, photomicrograph of Jacqueline's kidney. Most glomeruli are changed to a hyaline scar.

subacute glomerular nephritis. There was marked proliferation of capsular epithelium forming crescents. The capillary tufts, too, were cellular and avascular (Fig. 7). The tubules in both cases were atrophied. Some were dilated or cystic. There was an interstitial inflammatory reaction with fibroblastic proliferation and scattered infiltrations of lymphocytes and plasma cells. This latter did not seem to be related to the cystine deposits.

Sections of the lower end of the femur (from the boy) showed an essentially normal epiphysial line, but in the medulla of the shaft there was active osteoclastic activity, the cancellous spaces were filled with a loose fibrous tissue, and the bony

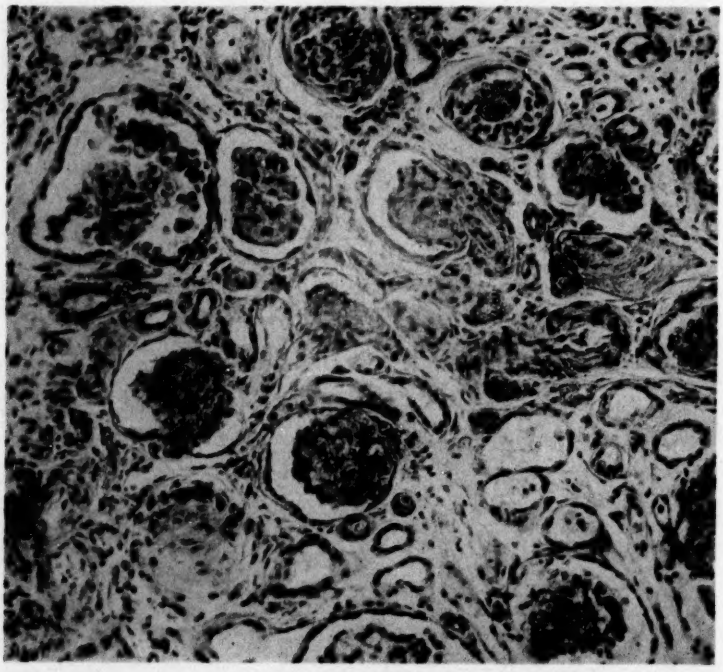

Fig. 7.—Photomicrograph of John's kidney. Increased cellularity and avascularity of the glomerular tufts and capsular proliferation and hyalinization of glomeruli are shown, also the atrophy and dilatation of tubules.

trabeculae were irregularly calcified with prominent cement lines. This resembled the changes seen in hyperparathyroidism. No cystine was seen in the bone marrow because the sections had been decalcified with acid.

Postmortem Diagnosis.—Primary lesion: cystinosis; secondary lesions: nephrosclerosis; hypertrophy of heart; passive hyperemia of lungs, liver, and spleen; hyperplasia of parathyroids; uremic pericarditis, and uremic enterocolitis.

A note concerning pathologic technique seems indicated. Most writers state that in order to preserve the cystine, the tissues should be fixed in absolute alcohol. Since, at the time of autopsy, the diagnosis in these two cases was not sus-

pected, this was not done. The tissues were fixed in formalin and in Zenker's fluid. The formalin-fixed sections still contained considerable cystine, but not nearly so much as did the Zenker's-fluid fixed sections. The latter apparently had lost none, since the cells remained packed with it.

The first sections prepared contained very little cystine, only the vacuolated large mononuclear leucocytes being left. This loss of the cystine proved to have occurred during the staining process, since unstained sections of the same blocks contained it in abundance. By modifying our hematoxylin-and-eosin staining process, omitting decolorization with hydrochloric acid, and omitting differentiation with ammonia, we obtained sections containing abundant cystine as illustrated in the photomicrographs. The tissues were embedded in paraffin using our routine old-fashioned alcohol-chloroform method.

COMMENT

Cystinosis appears to be a disturbance of protein metabolism which results in the deposition of the sulfur-containing amino acid, cystine, in the tissues. Freudenberg [5] suggests that cystinosis and cystinuria are manifestations of the same disturbance, age being the determining factor as to which form the disease takes. When cystine is fed to young rats, a glomerulonephrosis is said to develop, while in older animals it does not. Such rats do not have cystine deposits in the tissues. Hottinger's patient with cystinosis,[4h] who died of infection at 11 months, had no renal lesions. It therefore seems evident that the deposits in the tissues are not the result of disturbed renal excretion of cystine. Both cystinuria and cystinosis are familial, and both have been reported in the same family. The relationship between the two conditions, in our opinion, remains obscure. In our case, two examinations of 24-hour urine specimens of the father, mother, and sister were all negative for cystine.

The mechanism of the intractable rickets that accompanies cystinosis is also obscure. McCune and co-workers [6] suggest that perhaps the cystinosis is from the very beginning combined with acidosis. The acidosis by activating the alkaline phosphatase in the erythrocytes can cause a loss of phosphate in the urine resulting in hypophosphatemia quite apart from lack of vitamin D. The answer to this lies in the study of early cases before the renal failure brings about hyperphosphatemia and acidosis. In only one of the 17 cases recorded were there such early data. The patient in this one did have early acidosis. Both of our patients had acidosis and hypophosphatemia before there was evidence of renal failure. Later, the acidosis was less marked and the phosphorus greatly increased (Tables 2 and 3). The presence of early acidosis in all three cases so studied is fairly convincing evidence. It leaves us, however, with no explanation as to the genesis of the acidosis.

5. Freudenberg, E.: Cystinosis: Cystine Disease (Lignac's Disease) in Children, in Levine, S. Z., and others, Editors: Advances in Pediatrics, New York, Interscience Publishers, Inc., 1949, vol. 4, pp. 265-290.

6. McCune, D. J.; Mason, H. H., and Clarke, H. T.: Intractable Hypophosphatemic Rickets with Renal Glycosuria and Acidosis (Fanconi Syndrome): Report of Case in Which Increased Urinary Organic Acids Were Detected and Identified, with Review of Literature, Am. J. Dis. Child. **65**:81, 1943.

The renal lesions are likewise unexplained; we can only postulate that some precursor of the cystine is nephrotoxic, or perhaps an antigen-antibody mechanism is involved.

Once the diagnosis of this disease has been suspected from the clinical findings, there are valuable laboratory aids. The crystals are said to be visible in the conjunctiva by means of the slit lamp. A biopsy may be done on the conjunctiva and the cystine demonstrated histologically and chemically. Sternal biopsy is more practical, and the cystine may be demonstrated in the reticular cells of the sternal bone marrow. A lymph node may also be biopsied. When tissues are available for study, x-ray diffraction is useful in identifying the cystine. Occasionally, cystine may be found in the urine.

Cystinosis is probably not so rare as the paucity of case reports suggests. Twelve of the 17 cases recorded have been published since 1935. Because the cystine is soluble in acids and alkalies, it is liable not to be seen in preparations stained by routine techniques. The remaining large mononuclear cells with vacuolated cytoplasm may be misinterpreted. Some cases designated as renal rickets were perhaps cystinosis. As pediatricians and pathologists become aware of this disease and familiar with the proper techniques of clinical and postmortem diagnosis, an increasing number of case reports is to be anticipated.

DIPHENHYDRAMINE (BENADRYL) AND TRIPELENNAMINE (PYRIBENZAMINE) INTOXICATION IN CHILDREN

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AND
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IN VIEW of their widespread use in the therapy of allergic and associated disease, it seems wise to review the hazards of acute intoxication due to diphenhydramine (Benadryl) and tripelennamine (Pyribenzamine). The consumption of these agents has become enormous [1]; the associated hazards of indiscriminate use are the cause of great concern.[2] Toxic doses frequently cause many troublesome side effects and severe reactions, which can be the cause of death. This is our great concern. This paper will review the pharmacology and toxic manifestations of diphenhydramine and tripelennamine and will present two cases showing the divergent effects of severe central nervous system intoxication in children.

PHARMACOLOGY

Tripelennamine and diphenhydramine, when given by mouth, are completely and rapidly absorbed, but traces of the drugs can be found in the gastrointestinal tract four hours after administration.[3] The drugs rapidly leave the blood stream and localize in the various tissues. There is but a faint trace or an absence of tripelennamine and diphenhydramine in the blood stream 18 to 24 hours after a single oral dose.[4] Glazko and Dill [5] found in the rat that largest amounts of the drug are found in the lung, followed in order by the spleen, the liver, the brain, and the muscles. In the guinea pig they found the concentration was about the same, except that the concentration in the brain was greater than in the liver.

Read in part before the Colorado State Medical Society Meeting, 1952.

1. Antihistaminics for Colds, Editorial, J. A. M. A. **142**:570, 1950.

2. (*a*) Too Many Drugs, Council on Pharmacy and Chemistry, American Medical Association, J. A. M. A. **139**:378, 1949. (*b*) Antihistaminic Drugs Hazard to Children, Editorial, New York Med. **6**:14 (no. 3) 1950. (*c*) Risks of Antihistamine Medication, Editorial, Lancet **1**:28, 1950. (*d*) Feinberg, S. M.; Malkiel, S., and Feinberg, A. R.: The Antihistamines: Their Clinical Application, Chicago, The Year Book Publishers, Inc., 1950. (*e*) Wyngaarden, J. B., and Seevers, M. H.: The Toxic Effects of the Antihistaminic Drugs, J. A. M. A. **145**:277, 1951.

3. Way, E. L., and Dailey, R. E.: Adsorption, Distribution, and Excretion of Tripelennamine (Pyribenzamine), Proc. Soc. Exper. Biol. & Med. **73**:423, 1950.

4. Perlman, E.: Quantitative Method for the Determination of Antihistaminic Compounds Containing Pyridine Radical, J. Pharmacol. & Exper. Therap. **95**:465, 1949.

5. Glazko, A. J., and Dill, W. A.: Biochemical Studies on Diphenhydramine (Benadryl): Distribution in Tissues and Urinary Excretion, J. Biol. Chem. **179**:403, 1949.

Much of the action of tripelennamine and diphenhydramine may be due to their interfering with the action of histamine on the shock organs, i. e., mucous membrane, skin, conjunctivae, smooth muscle, etc.

The liver appears to be the principal site of diphenhydramine and tripelennamine degradation, although in the rat the lungs and kidneys are also active.[6] Very small amounts (1 to 6%) of administered diphenhydramine can be found unchanged in the urine. About 26 to 38% of the administered drug may be recovered from urine in the form of organic bases with the remainder unaccounted for in the urine.[7]

The concentration, particularly of tripelennamine, in the brain appears to be related to its toxic effects as observed in the rat.[8] Experimentally, diphenhydramine and tripelennamine do exert a selective inhibition on the respiration of slices of rat cerebral cortex when the latter are suspended in a medium containing *l*-glutamate.[8] Possibly tripelennamine and diphenhydramine interfere with the cellular permeability to oxygen or with the oxidation of *l*-glutamate. Hubbard and Goldbaum[9] demonstrated inhibition of glucose and pyruvate oxidation and of anaerobic glycolysis in mouse brain by tripelennamine. This may not explain the convulsant properties of tripelennamine or diphenhydramine but may account for its anesthetic and somnolent properties. Brain tissue contains very little histamine, and these reactions were not prevented nor reversed by the addition of histamine.[8]

TOXIC REACTIONS AND CLINICAL MANIFESTATIONS

Common side reactions of the antihistaminic agents are familiar to most physicians and will not be reviewed here. We are concerned primarily with the severe reactions and specifically those severe reactions which affect the central nervous system. Acute toxicity of the antihistaminic agents in the human will affect the gastrointestinal, cardiovascular, respiratory, genitourinary, and hematologic systems and the skin and the mucous membranes. However, neuropsychiatric manifestations are more frequent and important. The table, modified from Sachs,[10] lists the neurological and psychiatric reactions that have been observed.

The incident of side effects range between 10 and 63%.[11] The most severe reactions occur with higher doses. However, a severe toxic reaction does not depend on dosage, and the question of the patient's idiosyncrasy to one of the drugs is important.

About half of the 30 cases of severe intoxication reported have been in infants and children. Children are more susceptible to the stimulatory effects of these drugs,

6. Glazko, A. J., and Dill, W. A.: Biochemical Studies on Diphenhydramine (Benadryl): Degradation of Benadryl by Tissue Enzymes, J. Biol. Chem. **179**:417, 1949.

7. Glazko, A. J.; McGinty, P. A.; Dill, W. A.; Wilson, M. L., and Ward, C. S.: Biochemical Studies on Diphenhydramine (Benadryl): Application of Radioactive Carbon to Metabolic Studies of Benadryl, J. Biol. Chem. **179**:409, 1949.

8. Carlisle, E. M., and Crescitelli, F.: Selective Inhibition of Brain Respirations by Benadryl, Science **112**:272, 1950.

9. Hubbard, T. F., and Goldbaum, L. R.: Effects of Pyribenzamine on Respiration of Mouse Brain Homogenates, J. Lab. & Clin. Med. **35**:284, 1950.

10. Sachs, B. A.: The Toxicity of Benadryl: Report of a Case and Review of the Literature, Ann. Int. Med. **29**:135, 1948.

11. Feinberg.[2d] Wyngaarden and Seevers.[2e] Lecks, H. I.: Acute Antihistamine Intoxication in Childhood, Quart. Rev. Pediat. **6**:294, 1951. Sachs.[10]

although depression can occur. The question of idiosyncrasy and the great variation in tolerance [12] to dosage make antihistamine intoxication a real problem, as will be described. It is thought that toxic reactions are more common in the allergic person.

There is similarity between the atropine- and the antihistamine-intoxicated child. The effects on the central nervous system involve both the cerebrum and cerebellum with initial stimulation followed terminally by depression. Cortical stimulation can be intense. Hallucinations, excitement, muscular tremors, athetoid movements, and ataxia can occur. Muscular twitching and athetoid movements often will precede convulsions which are of the tonic-clonic type and exceedingly refractory to treatment. The initial stimulatory effects are often accompanied by dilated pupils, flushed facies, and hyperpyrexia. Vomiting is uncommon in children, and perhaps if it did occur it might lessen the degree of poisoning. The critical period following the ingestion of excessive amounts of the drugs is about two to eight hours. Following this critical period, the symptoms and signs frequently resolve. In fatal cases, convulsions are followed by coma and cardiorespiratory

Neurological and Psychiatric Toxic Reactions

A. Central	Weakness	4. Miscellaneous
1. Stimulation	Ataxia	Fever
Insomnia	Delirium	Hyperthermia
Nervousness	Coma	Electroencephalogram changes
Vagal stimulation	3. Neuropsychiatric	B. Peripheral
Tachycardia	Nightmares	Toxic neuritis
Hypertension	Poor judgment	Paresthesias
Muscular twitching	Delusions	Paralysis
Hyperreflexia	Hallucinations	Areflexia
Tremor	Confusion	C. Special Senses
Convulsions	Toxic psychosis	Tinnitis
2. Depression	Dizziness	Vertigo
Drowsiness	Headaches	Blurring vision
Somnolence	Syncope	Dilated pupils
Narcolepsy	Cerebral edema	

failure. Complicating renal and hepatic disease may occur in severe poisoning. In a few fatal cases autopsy findings have been likened to those found in heat stroke.[13] Anoxic changes in the brain, liver, lungs, and kidneys have been reported.[2e]

Case 1.—A 2½-year-old girl who had previously been in good health was suddenly observed to be in a highly nervous fretful state. Shortly thereafter she became disoriented and walked with a staggering awkward gait. On investigation, the contents of a bottle of 50 mg.-capsules of diphenhydramine were found with about 10 capsules missing. The time of ingestion was approximately one hour earlier. The youngster was immediately brought to the hospital where gastric lavage was carried out. At this point the youngster showed extreme stimulation with hallucinations, muscular twitchings, hyperreflexia and intermittent tremors. She was completely disoriented. After extensive lavage a considerable amount of material which resembled the capsule and the contents of the capsule of the ingested agent was identified in the washings. Sodium phenobarbital was hypodermically administered.

Examination at that time, approximately three hours after the ingestion, revealed a small well-developed well-nourished white child who had accentuation of the central nervous system stimulatory effects mentioned previously, with the muscular twitching aggravated and with frequent athetoid movements. Neurologic examination, including funduscopic, revealed only a generalized bilateral hyperreflexia. The pupils were dilated and fixed. There were no abnormal

12. Weil, H. R.: Unusual Side Effect from Benadryl, J. A. M. A. **133**:393, 1947.

13. Davis, J. H., and Hunt, H. H.: Accidental Benadryl Poisoning: Report of a Fatal Case, J. Pediat. **34**:358, 1949.

peripheral neurologic signs. The only other positive physical findings were a pulse rate of 165, a rectal temperature of 99.8 F., and a blood pressure of 76/48. The youngster was placed in an oxygen tent and wrapped in ice cold sheets. Sodium phenobarbital was administered hypodermically and the dose of the drug cautiously repeated at intervals during the first three hours of observation following the lavage. Two and one-half grains of phenobarbital were administered during this period. At the end of that time ¾ grain of secobarbital (Seconal) was administered and repeated in one and one-half hours, making the total dosage in five and one-half hours 2½ grains phenobarbital and 1½ grains seconal. At this point her general excitability seemed lessened, although the athetoid movements persisted. There was no change in the physical findings. Shortly thereafter the child fell into a restless sleep which lasted about five hours. She was given quantities of dextrose solution administered parenterally.

About 14 hours after the ingestion of the material, the central nervous system stimulatory effects were lessened, and there were no abnormal peripheral neurologic signs. Hyperreflexia still existed, and hallucination and confusion were noted intermittently. Temperature elevation of 102 F. (rectal) developed, and a prophylactic dose of penicillin was given. The fever persisted for the next 12 hours. One grain of phenobarbital was given every six hours. Ten per cent dextrose content solution, as desired, was given orally with a high carbohydrate diet.

Thirty hours after the ingestion the child was talkative, but apparently normal physically and mentally and without fever. She was discharged from the hospital and gradually returned to a completely normal state.

This case represents a severe toxic reaction to the ingestion of approximately 500 mg. of diphenhydramine. It is interesting to note that this child had a past history of allergy. The effects on the central nervous system seem to be more common in large dosages with intoxication usually occurring with a single large dose. Borman [14] reported the case of an adult ingesting 2,000 mg. of diphenhydramine with resultant disorientation, confusion, and lethargy. Complete recovery ensued in 48 hours. Weil [12] reported the severe effect in an adult who took 100 mg. of diphenhydramine with toxic manifestations consisting of excitement, hilarity, muscular twitchings, and involuntary movements of the extremities. Hyperpyrexia, a common finding in these cases, was present. The number of instances of recovery from excessive doses of antihistaminic agents is slightly greater than the number of deaths.[2e]

Case 2.—A 2-year-old white child was hospitalized on Feb. 1, 1952, because of sudden onset of extreme weakness. Three days prior to the onset of this illness the child developed a mild cold with cough and rhinorrhea. The latter improved and the night prior to admission the child seemed quite well. Upon arising the following morning the child was unable to walk and seemed very sleepy. She had vomited her breakfast and felt feverish. She was taken to her local physician, who then referred her to one of us (K. W. D.). Upon questioning of the parents, it was determined that she had taken two 50-mg. tablets of tripelennamine. She had had but the one episode of vomiting following the drug ingestion and no other signs or symptoms were noted by the parents. The child had been in good health up to this time.

Physical examination at the time of admission revealed a well-developed well-nourished extremely lethargic and ataxic white child. Temperature was 99.4 F., pulse rate 130, respirations 20, blood pressure 64/42. She was unable to stand, even with support, and upon sitting with support she seemed to continually fall to the right side. There was an unsustained coarse horizontal nystagmus. Her pupils were widely dilated and reacted sluggishly to light. The fundi were easily visualized and were perfectly normal. There was a small amount of serous discharge from the nose. The pharynx was mildly inflamed and slightly granular. The most impressive

14. Borman, M. C.: Danger with Benadryl of Self Medication and Large Dosage, J. A. M. A. **133**:394, 1947.

findings were limited to the neurological examination, i. e., a coarse horizontal nystagmus and marked generalized hypotonia with severe ataxia. The deep tendon reflexes were all extremely hypoactive. The superficial abdominal reflexes were present.

Laboratory work revealed the following: 11 gm. of hemoglobin per 100 ml. of blood; 4,360,000 red blood cells per cubic millimeter, and 9,750 white blood cells per cubic millimeter, with a predominance of polymorphonuclear cells. The urine when tested showed a strongly positive reaction to acetone. The throat culture revealed predominantly a hemolytic Streptococcus. Results of an examination of the cerebrospinal fluid were normal, and a blood culture was normal. Roentgenograms of the skull were normal.

A tentative diagnosis of antihistamine poisoning was made. Because of the extreme lethargy the child was given 1 grain of caffeine with sodium benzoate intramuscularly, which was repeated in four hours, without appreciable effect. There was no change after the intramuscular administration of 0.5 mg. of neostigmine (Prostigmin) methyl bromide. Over the next 24 to 36 hours additional small injections of caffeine with sodium benzoate were given with very little response. Over the following two-day period the child's condition was unchanged. She remained extremely lethargic and weak, was unable to turn over without assistance, and when placed in a sitting position she fell to the right side. After the second day the child improved gradually. Her strength returned, the ataxia and nystagmus gradually disappeared, and she seemed to take more interest in her surroundings. By the fourth hospital day the child was able to sit and stand fairly well. She could answer questions; the reflexes were more active. She was still ataxic but was able to walk a short distance. By the sixth hospital day she appeared fully recovered from the effects of the overdose of tripelennamine. On the sixth day her temperature spiked at 101 F., and examination at that time revealed an inflamed and granular pharynx. The child was given penicillin intramuscularly with favorable response in 24 hours, at which time she was discharged.

This case greatly resembles that of Schwartz.[15] Because of the child's age, tinnitus could not be determined. It is possible that an acute labyrinthitis cerebellar dysfunction may have developed in this child.

TREATMENT

Treatment of intoxication due to tripelennamine and diphenhydramine depends upon the type of reaction encountered, and without a specific antidote, it is entirely symptomatic. In the therapy of allergic disorders with the drugs under discussion, the dosage of the drug should be adjusted to the patient's needs and should be prescribed in small amounts and not be given over a long period of time without reevaluation of the patient's situation. The recommended maximum dosage of antihistamines for children is 2 mg. per pound (0.5 kg.) of body weight.[16] In the treatment in a case of excessive ingestion, an initial evacuation of the contents of the stomach should be attempted. It is not recommended that this be done in any way other than by the mechanical method because of the danger of aspiration of the stomach contents. When evidence of central nervous system irritation is present, the barbiturates should be administered cautiously as needed. Although it would seem that one should avoid the accumulative effects of sedatives and use shorter acting barbiturates, phenobarbital with its specific anticonvulsive effect seems to be most useful. When convulsions occur they can be treated by large doses of sedatives and probably best controlled by ether or paraldehyde. When depressant effects are substituted for the excitatory effects, amphetamine sulfate (Benzedrine) or caffeine can be given either intramuscularly or intravenously. The dosage and method of

15. Schwartz, E.: Comparative Toxicity and Side Effects of the Antihistaminic Drugs, Ann. Allergy **7**:770, 1949.

16. Logan, G.: Personal communication to the authors.

administration depend on the age of the child and the degree of intoxication. It is obvious that the medications used, either sedative or stimulant, can augment the toxic effects of the antihistaminics. The necessity of very close observation of the patient, preferably by a physician, cannot be emphasized too thoroughly. Oxygen permits more comfort and easier breathing. Fluids, including dextrose solutions, can be used as indicated.

CONCLUSIONS

Accidents lead the list of causes of death and disability among children. The accidental ingestion of medicine is a type of accident often encountered. Because of the widespread use of the so-called antihistaminic drugs instances of poisoning by one of these drugs are being encountered. Treatment of these and other household accidents is largely ineffective and prevention of the accident the best therapeutic measure. Experience shows only several antihistaminic agents capable of causing convulsive deaths in children, but, judging from the experimental data, one should expect that the majority of the agents are capable of producing the same effects.

209 S. Nevada Ave. (Dr. Judge).

Case Reports

LYMPHOSARCOMA OF THE CECUM CAUSING INTUSSUSCEPTION IN A NINE-YEAR-OLD BOY

JOHN ERBES, M.D.
AND
JOHN S. STEHLIN Jr., M.D.
MILWAUKEE

INTUSSUSCEPTION is generally considered to be a condition of infancy and early childhood and is usually of the idiopathic type. Intussusception in older children and adults is less common and a causative factor such as a tumor, Meckel's diverticulum, or a foreign body can usually be determined.

Few cases of lymphosarcoma of the cecum causing intussusception have been reported. We would like to add another case to the literature.

This case was interesting from the standpoint of diagnosis and treatment. It is not being presented as a "cure," although no malignant disease could be demonstrated at reoperation. We feel that the second-look procedure was indicated in this case, and should be employed more frequently in certain selected cases.

REPORT OF CASES

The patient was a white boy, aged 9 years, who was admitted to the medical service of Milwaukee Children's Hospital on Jan. 3, 1952. He complained of abdominal pain which had been present one month. Pain was periumbilical in location, came on about 30 minutes following each meal, and lasted a few minutes. Several days before admission, these painful episodes became more severe. He had vomited only twice. Bowel habits were regular, and stools did not appear abnormal. He had lost 5 lb. (2.3 kg.) in the month prior to admission. Past history revealed that the mother was informed three years before admission that this child had a heart murmur.

On admission to the hospital, the initial examination revealed a well-developed, undernourished, pale, white boy, who did not appear acutely ill. His temperature and pulse were normal. A systolic murmur was heard at the apex. Findings on examination of the abdomen were normal. The results of his physical examination were otherwise essentially normal.

Findings on the immediate laboratory studies, including hemoglobin concentration, white blood cell count, differential count, sedimentation rate, and urinalysis were normal. The electrocardiogram did not show any significant changes.

Within 36 hours following admission this child began to have attacks of severe abdominal pain. At this time, a mass, which was slightly tender, was palpated above and just to the right of the umbilicus. He was seen by the surgical service. A survey film of the abdomen showed no evidence of intestinal obstruction. There was, however, a soft tissue shadow in the upper middle abdomen of undetermined origin. An intravenous pyelogram revealed normal function of both kidneys with no pathology. Barium enema examination revealed intussusception at about the middle of the transverse colon.

He was taken to surgery, and a transverse incision 1 in. (2.5 cm.) above the umbilicus was made. Ileocolic intussusception was found, the intussusceptum being in the middle portion of the transverse colon. The ileum was easily reduced. However, the cecum presented a rather

From the Surgical Service (Dr. Erbes), Surgical Resident (Dr. Stehlin), Milwaukee Children's Hospital.

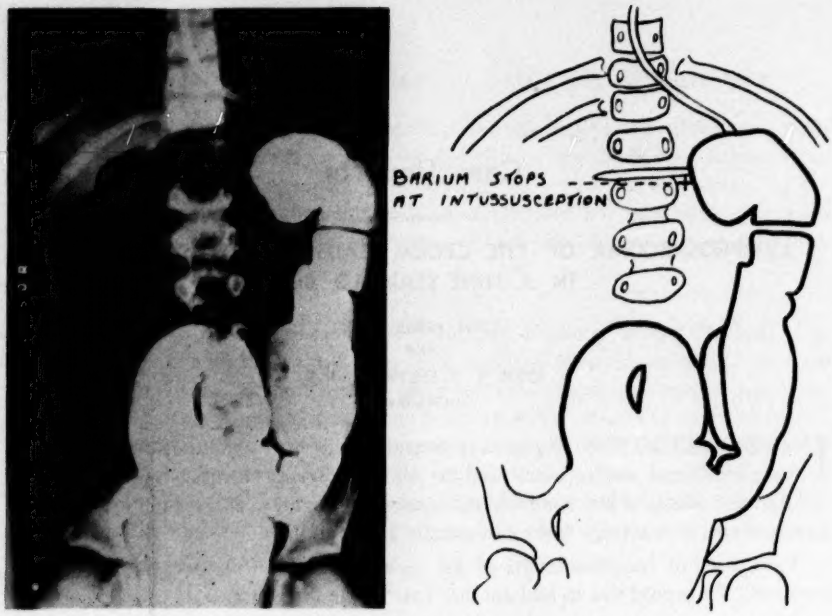

Fig. 1.—Barium enema showing intussusception.

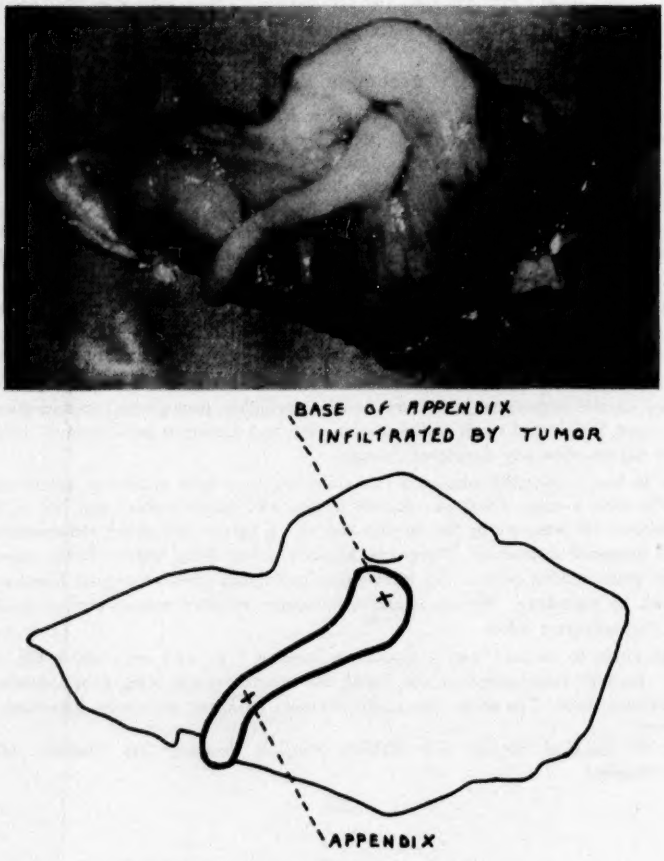

Fig. 2.—Base of appendix infiltrated with tumor.

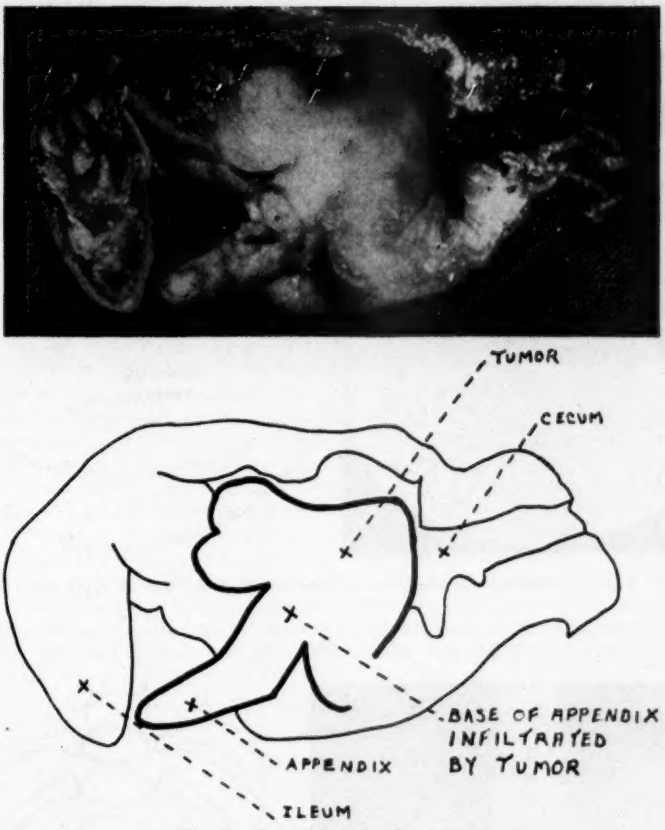

Fig. 3.—Cut section showing tumor.

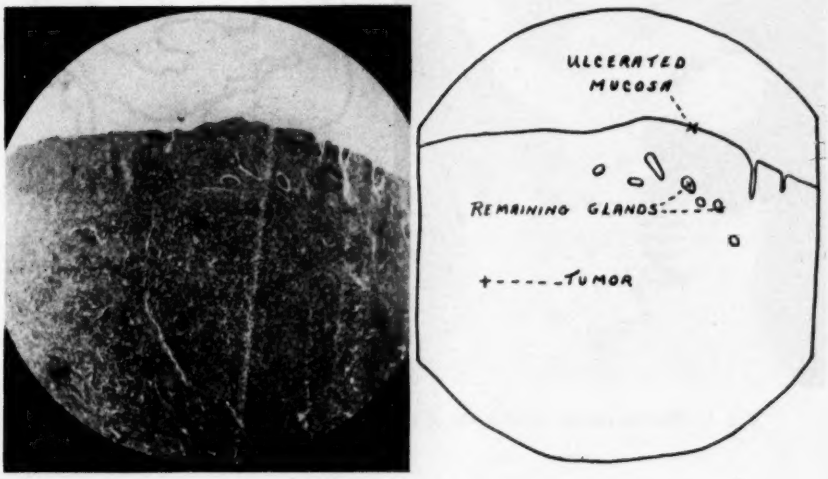

Fig. 4.—Tumor of cecum (photomicrogram).

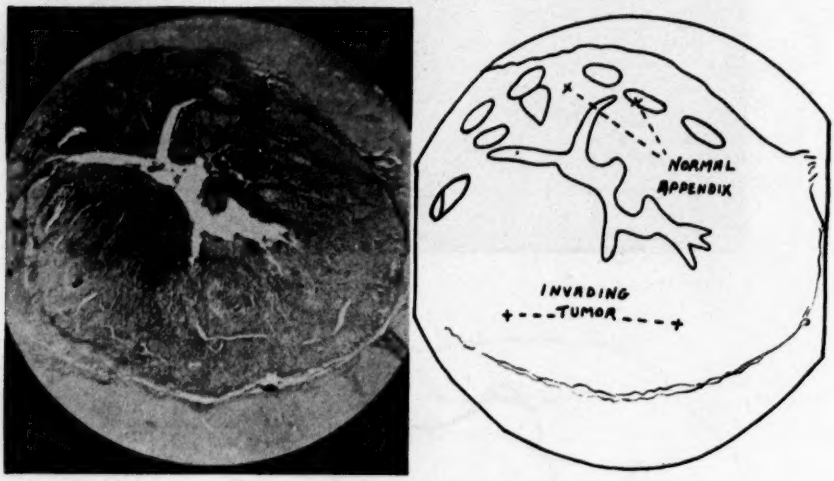

Fig. 5.—Photomicrogram showing tumor infiltrating base of appendix.

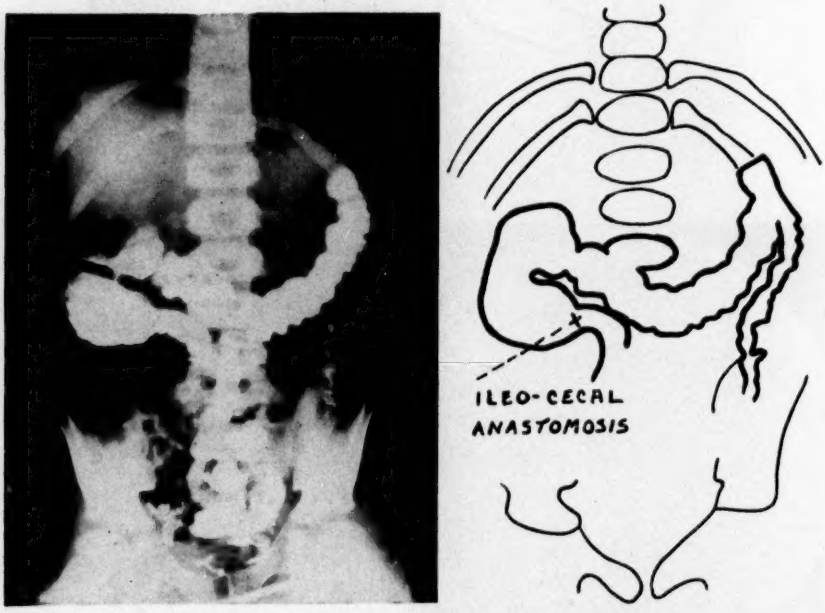

Fig. 6.—Barium enema showing site of anastomosis four months postoperatively.

unusual appearance. It appeared as if the base of the appendix and the corresponding portion of the cecum had been sucked into the distal portion of the cecum. A mass measuring about 1¼ in. (3 cm.) in diameter and firm in consistency could be felt through the wall of the cecum in the appendiceal-cecal region. It was impossible to reduce completely the base of the appendix which had intussuscepted into the cecum itself, even though the ileum could be reduced completely. Some of the lymph nodes in the ileocecal region as well as the mesentery of the right colon measured upwards to 3 cm. in diameter. A resection of the ileocecal region, including 3 in. (7.6 cm.) of the terminal ileum, the cecum, and 3 in. of the right colon, was done. An open type end-to-end ileocolic anastomosis was accomplished.

Postoperatively partial small intestinal obstruction developed which responded promptly to intestinal tube decompression. The recovery otherwise was satisfactory. The pathologist reported this lesion to be lymphosarcoma involving the cecum and the adjacent base of the appendix. Radiotherapy was begun on the 17th postoperative day and continued for eight days. A total of 1,000 r was given in divided doses to the entire abdomen.

The patient's convalescence at home was gratifying. His appetite was good, and he gained weight. He was readmitted to this hospital four months following the initial operation in apparently excellent health. The results of the physical examination were normal. Barium enema examination revealed a well-functioning ileocolic anastomosis. Intravenous pyelogram, roentgenogram of the thorax, peripheral blood studies, and sedimentation rate were normal. The surgeons felt the patient possibly could benefit from reoperation even though there was no evidence of recurrence. It was their opinion that the original inflammatory process had subsided. If a tumor could be demonstrated it was hoped either more definitive surgery could be done or more efficient radiotherapy could be administered to a smaller field. Accordingly, a second-look procedure was performed. Abdominal exploration failed to reveal any evidence of recurrence. The lymph nodes at this time appeared negative. Appropriate biopsies did not demonstrate any malignancy. His convalescence was uneventful, and he was discharged on the eighth postoperative day.

PERIARTERITIS NODOSA

Report of a Case of Apparent Recovery in a Nine-Year-Old Boy During Cortisone Therapy

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AND
DOROTHY J. YORK, M.D.
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PERIARTERITIS nodosa has no typical course. It resembles various other diseases and is seldom proved during life. It is therefore an alternative to be considered in diagnosing many of the illnesses of childhood.[1]

Analyzing 42 cases of periarteritis nodosa in children (as found in the literature) Keith and Baggenstoss [2] listed the following symptoms in order of frequency: fever, usually intermittent; leucocytosis; abdominal pains; rheumatic pains; renal disease; general weakness; convulsions; tachycardia; anemia; purpuric rash; other rashes, chiefly urticaria; hypertension; tonsillitis or sore throat; headaches; intestinal hemorrhage; peripheral gangrene; signs of meningeal irritation; palpable nodules.

The small number of cases recorded (less than 500 among adults, less than 60 among children) may be attributed partly to the rarity of the disease and partly to the difficulties of recognition. Even when diagnosis is established, death usually follows. No specific therapy is known.

In this disease of the smaller arteries and veins, lesions may occur in any organ, giving rise to a variety of symptoms. Since the condition was first defined in 1866

The cortisone used in treating this patient was purchased with money given by the school children of Laurel, Miss., at the request of the Indian Springs Baptist Church, Route 5.

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1. (*a*) Rothstein, J. L., and Welt, S.: Periarteritis Nodosa in Infancy and Childhood: Report of 2 Cases with Necropsy Observations; Abstracts of Cases in Literature, Am. J. Dis. Child. **45**:1277-1308, 1933. (*b*) Boyd, L. J.: The Clinical Aspects of Periarteritis Nodosa, Bull. New York M. Coll. **3**:32-40, 1940.

2. Keith, H. M., and Baggenstoss, A. H.: Primary Arteritis (Periarteritis Nodosa) Among Children, J. Pediat. **18**:494-506, 1941.

by Kussmaul and Maier,[3] information regarding its effects has been provided by Arkin,[4] Etinger and Vilk,[5] Lamb,[6] Wold and Baggenstoss,[7] and others.

Recognition in children has occasionally been made possible by the reports, analytical studies, and summaries of Rothstein and Welt,[1a] Keith and Baggenstoss,[2] Klein,[8] Ward,[9] Branch and Roberts,[10] and by various studies not restricted to any age group.

The following case (in which diagnosis was established through biopsy during the 31st month of illness) is of unusual interest because of its duration (periarteritis nodosa is usually of brief duration in children) and because of the patient's dramatic response to cortisone and apparent recovery after other therapies had failed. There has been opportunity to observe this patient for two years since the completion of cortisone therapy.

REPORT OF CASE

H. H., a chronically and acutely ill 9-year-old boy, was referred to us on Feb. 6, 1950. A history of measles, pertussis, chicken pox, mumps, and tonsillitis was given, and the parents stated that the patient "almost always had a cold." He had not received any of the usual immunizations against childhood diseases. The mother had hay fever and asthma. Otherwise the family history was noncontributory.

Present Illness.—For two and one-half years the patient had complained of abdominal discomfort and recurrent pains in the muscles and joints. Intermittent fever and episodes of dermatitis had occurred repeatedly. Initially urticarious, often the dermatitis had become hemorrhagic before gradually disappearing in two to three weeks. Spotty gangrene of the fingers had appeared from time to time. The distal phalanx of the right index finger showed a partial gangrenous slough. A rash and edema had followed the administration of sulfonamides. Weakness and weight loss had progressed, and for 30 months the child's health had gradually declined. Three months of bed rest and a variety of therapies, including sulfonamides, streptomycin, and penicillin, had failed to check the decline.

Physical Examination.—The initial examination on Feb. 6 revealed an emaciated apprehensive acutely and chronically ill boy. The weight was 35 lb. (15.9 kg.). The temperature was 101 F. (oral), pulse rate 120 per minute, and respiration 28 per minute. The blood pressure was 90/60. Lymphadenopathy was generalized. Small ill-defined subcutaneous nodules were palpable over the abdomen, which was protuberant and rigid. Veins over the abdomen and thorax were strikingly visible. The teeth and tongue were discolored, presumably the result of iron therapy.

3. Kussmaul, A., and Maier, R.: Über eine bisher nicht beschriebene eigenthümliche Arterienerkrankung (periarteritis nodosa), die mit Morbus Brightii und rapid fortschreitender allgemeiner Muskallähmung einhergeht, Deutsches Arch. klin. Med. **1**:484-518, 1866.

4. Arkin, A.: A Clinical and Pathological Study of Periarteritis Nodosa: A Report of Five Cases, One Histologically Healed, Am. J. Path. **6**:401-426, 1930.

5. Etinger, Y. G., and Vilk, N. L.: Pathology and Clinical Features of Periarteritis Nodosa, Klin. med. **26**:31, 1948.

6. Lamb, A. R.: Periarteritis Nodosa: A Clinical and Pathological Review of the Disease with a Report of 2 Cases, Arch. Int. Med. **14**:481-516, 1914.

7. Wold, L. E., and Baggenstoss, A. H.: Gastrointestinal Lesions of Periarteritis Nodosa, Proc. Staff Meet., Mayo Clin. **24**:28-35, 1949.

8. Klein, S. P.: Periarteritis Nodosa: Study of Chronicity and Recovery; with Report of 2 Cases, Arch. Int. Med. **84**:983-1001, 1949.

9. Ward, R.: Periarteritis Nodosa, in Brennemann, J.: Practise of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1948, Vol. 3, Chap. 13, p. 71.

10. Branch, L. K., and Roberts, M. H.: Periarteritis Nodosa: A Report of a Case with Clinical Diagnosis, A. M. A. Am. J. Dis. Child. **81**:788-797, 1951.

The tonsils were enlarged and hyperemic. The retinas of both eyes appeared to be normal. The disks were not well visualized, as the child did not cooperate. Examination of the heart disclosed tachycardia and a soft systolic apical murmur. Otherwise, the heart appeared normal. Fine moist rales were present at both lung bases. Dermal and muscular atrophy (associated with prolonged bed rest) had caused flexion contractures of both legs. The patient was unable to turn his head or flex his neck. The knees were flexed on the abdomen. Positive Kernig and Brudzinski signs suggested neurologic involvement. The child had been unable to walk for three months.

Laboratory Examination.—On admission, the urinalysis revealed a trace of albumin and rare red blood cells. The blood cell count showed 2,700,000 erythrocytes, with hemoglobin concentration of 7.0 gm. per 100 cc. The white cell count was 19,000, of which 80% were neutrophiles (75% segmented cells), 3% eosinophiles, 15% lymphocytes, and 2% monocytes. The total blood proteins were 8.00 gm. per 100 cc., with an albumin-globulin ratio of 3.57 : 4.43. Serum calcium was 10 mg. per 100 cc.; phosphorus was 6.08 gm. per 100 cc. Blood metabolites and glucose were normal; the blood culture was sterile. The erythrocyte sedimentation rate (Wintrobe, corrected) was 32 mm. in one hour. Gastric analysis evidenced 10 degrees total and 4 degrees free hydrochloric acid and a trace of occult blood. The intradermal reaction to old tuberculin 1 : 1,000 was 4+. Gastric washings and sputum cultured for tubercle bacilli were negative. A marrow biopsy demonstrated essentially normal tissue, except for a very slight shift to the left of the granulocytes and a slightly lowered proportion of nucleated red blood cells. Roentgenologically, the bones of the skull, thorax, and extremities appeared to be normal. An x-ray examination of the chest disclosed no abnormality of the lungs. The electrocardiogram showed no abnormality of the heart.

Clinical Course in Hospital Prior to Diagnosis of Periarteritis Nodosa.—Treatment during the first three weeks of hospitalization was symptomatic. Aureomycin hydrochloride, salicylates, vitamins, and transfusions of whole blood maintained normal temperature for two weeks and effected a weight gain of 15 lb. (6.8 kg.). The patient became able to sit up in a wheel chair. He did not regain the ability to walk. On the 16th hospital day, he complained of malaise and generalized pain, particularly in the joints. Most of the original symptoms of his illness returned. The temperature rose to 102 F. (oral). Areas of indurated erythema appeared on the body surfaces and extremities. A biopsy study of a lesion from the abdomen (taken during the 132d week of illness) revealed the classic vascular lesions of acute periarteritis nodosa (Fig. 1).

Precortisone Laboratory Examination.—Before cortisone was administered, the following reports were obtained. The urinalysis revealed a trace of albumin and rare red blood cells. The hemoglobin concentration was 8.7 gm. per 100 cc. with 3,630,000 erythrocytes, 18,700 white cells, and a differential count of 65% neutrophiles, 3% eosinophiles, 28% lymphocytes, and 4% monocytes. The thrombocyte (platelet) count was 333,600. The sedimentation rate (Wintrobe, corrected) was 32 mm. in one hour. Venous clotting time was 5 minutes. The total blood protein was 7.33 gm. per 100 cc., with an albumin-globulin ratio of 3.62 : 3.71. The blood culture was sterile. The nonprotein nitrogen level was 25.8 mg. per 100 cc., with a creatinine level of 1.5 mg. per 100 cc. Urea was 12.9 mg. per 100 cc. Gastric washings and sputum cultured for tubercle bacilli repeatedly gave negative reactions. X-ray examination of the chest revealed no abnormality of the lungs and showed the heart and great vessels to be within normal limits. The patient's weight was 50 lb. (22.7 kg.). See Figure 2.

Course.—On Feb. 27 at 8 a. m. the temperature was 102 F. (oral). The blood pressure was 98/48. The patient was given 100 mg. of cortisone (Cortone) administered intramuscularly at 8 : 15 a. m. and again at 4 p. m. A dose of 5 grains of acetylsalicylic acid was given at 8 : 30 a. m. and this amount was repeated every three hours to a total of 20 grains during the day. No other medication was given. By noon of the first day of this therapy the temperature had dropped to 98.0 F. and the generalized pain had begun to diminish. By 6 p. m. the temperature had risen to 101 F., but the boy was more comfortable and could move his joints without pain for the first time in approximately two years.

Use of cortisone and acetylsalicylic acid was continued on the second day in the same amounts and on the same schedule as on the first. The patient continued to be comfortable, and a mild euphoria developed. At 6 p. m. the temperature was 99.2 F. The blood pressure was 100/70.

Fig. 1.—Vascular lesion characteristic of periarteritis nodosa in the subcutaneous tissue of the abdomen, taken before cortisone therapy was initiated. Note the swelling and acute inflammatory reaction in the arterial wall. The endothelium was swollen and the lumen was greatly diminshed in size. Hematoxylin and eosin; × 400.

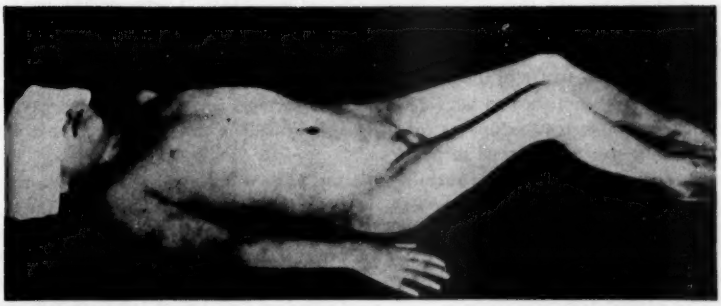

Fig. 2.—During the 31st month of illness, prior to cortisone therapy, the muscles of the legs were atrophied and the knees were flexed, as the child had been unable to walk for three months. Areas of indurated erythema were apparent on the body surfaces and extremities. The patient's weight was 50 lb. (22.7 kg.).

On the third day, the patient took a few steps for the first time in four months, although he was not able to straighten his knees completely. The temperature was 98.0 F. The blood pressure was 122/88. Administration of 20 grains of acetylsalicylic acid per day was continued. Cortisone was reduced to 100 mg. per day, in doses of 50 mg. each.

The boy's appetite became much greater than that of the average child, and by the seventh day he had gained 4 lb. 2 oz. (1.8 kg.). However, there was no evidence of fluid retention or edema, and a salt-free diet was not indicated. The hemoglobin concentration had risen to 10.8 gm. per 100 cc. The blood cell count showed 4,000,000 red cells, with white cells reduced to 50% of precortisone values. The urine was free of albumin. The patient was now receiving 50 mg. of cortisone per day in doses of 25 mg. each.

Moon-shaped facies were first observed in the patient on the 10th day; afebrile and free of pain, he spent most of his time walking around the hospital corridors or playing in the ward. Acetylsalicylic acid treatment was discontinued. Administration of 30 drops per day of a multivitamin compound (Vi-Syneral) was started and continued until the patient was discharged from the hospital. On the 15th day administration of 20 drops per day of a vitamin B compound (Multibeta) and administration of vitamin C were started and continued throughout the course of hospital therapy (Fig. 3).

A slight hypertrophy of the breasts was noted on the 16th day. This was nonpainful, and did not increase. On the 18th day an exacerbation of the disease occurred with a sudden rise in temperature to 104 F. For six days cortisone was administered in the increased amount of 100 mg. per day, during which time the manifestations subsided and the temperature returned to normal. During the fifth and sixth weeks, while being maintained on 25 mg. of cortisone per day, the patient was increasingly active.

On the 45th day, he complained suddenly of severe pains in the right lower quadrant of the abdomen. The possibility of acute appendicitis made laparotomy seem advisable. Surgery revealed no gross abnormalities but a mildly inflamed appendix and a few scattered small nodules in the mesentery. For biopsy study, a nodule was taken from Camper's fascia just under the skin in the upper extremity of the wound. The report from the pathologist (No. S-50-1467, April 13, 1950, Southern Baptist Hospital) stated:

"Section through the tissue labelled 'biopsy of skin nodule' shows it to consist of lobules of adult fat which are separated by thin strands of connective tissue. A number of small interlobular blood vessels are noted, some of which show slight increase in the surrounding connective tissue that contains a few lymphocytes. There appears to be a slight endothelial proliferation in some of these vessels and in some instances the surrounding proliferation of connective tissue appears to show some hyalin change. There is no obliteration of any of the vessels noted. Diagnosis: healing periarteritis of the skin."

During anesthesia, the patient had an unexplained convulsion. Cortisone was increased to 100 mg. per day for three days following the operation. Except for a retarded healing of the incision, the postoperative course was uneventful. Within a few days, the patient was up and about. There was no return of the pain (Fig. 4).

Cortisone was discontinued on the 55th day of this therapy, a total of 3.025 gm. having been given. Use of vitamin compounds was continued. No symptoms of adrenocortical atrophy were present, and the patient continued to improve.

Six days later, laboratory tests revealed that the urine was normal. The differential blood cell count, the blood chemistry, and the albumin-globulin ratio were within normal limits. The erythrocyte sedimentation rate was slightly elevated. The electrocardiogram revealed no abnormality. The temperature was 98.2 F.; the blood pressure 104/82; the weight 70 lb. (31.8 kg.). The patient was permitted to go home.

Physical examination at the time of discharge from the hospital disclosed the following: The boy stood erect and was able to remove his clothes, including his shoes, without difficulty. He was mentally alert, and his emotional attitude was good. Approximately the full range of motion was present in all but the knee joints, and the impairment there was slight. The color and texture of the skin were good. The site of slough on the distal phalanx of the right index finger had completely healed. The veins over the thorax were slightly more prominent than normally. Although the cervical and inguinal lymph nodes were still palpable, the generalized

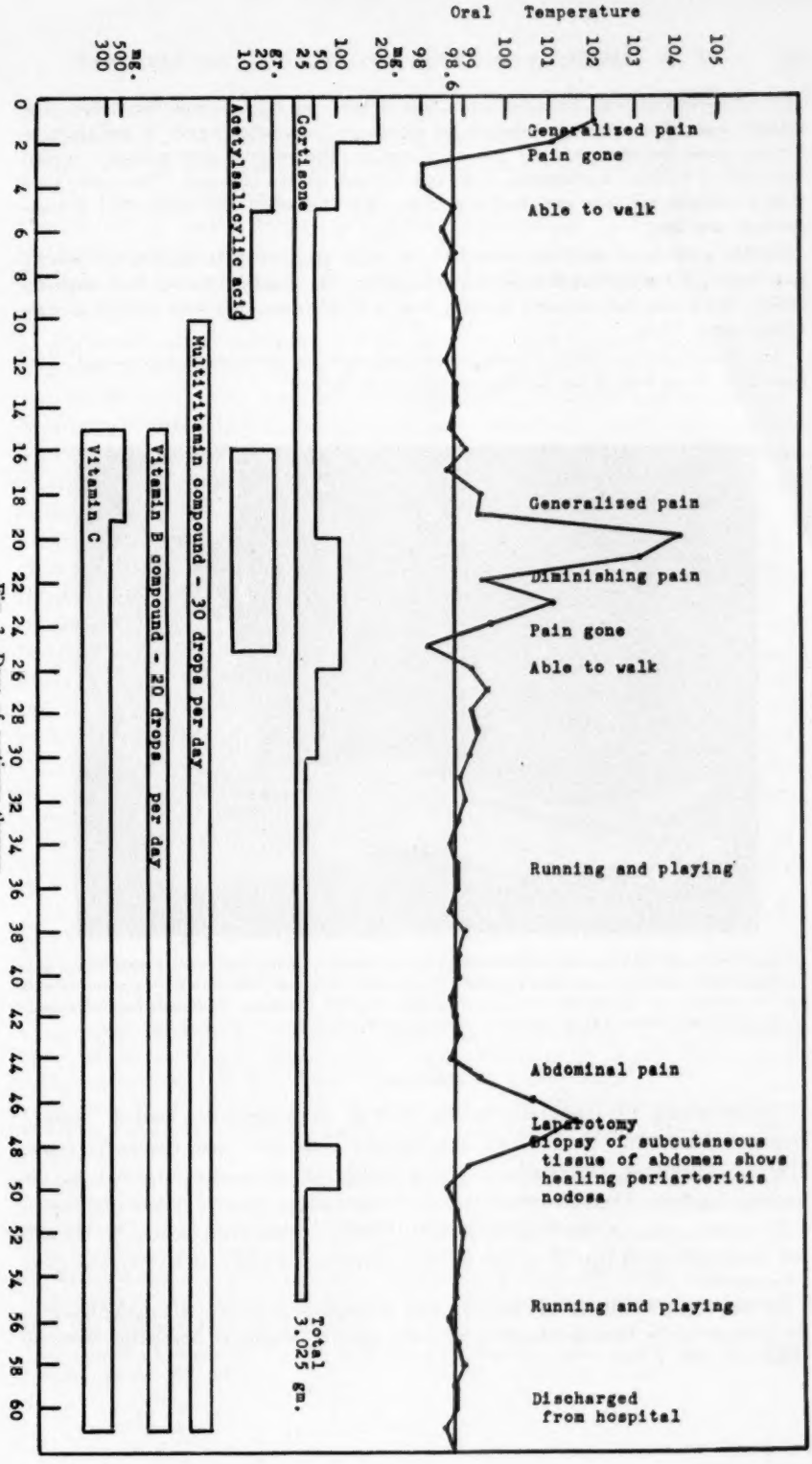

Fig. 3—Days of cortisone therapy.

adenopathy had decreased. Subcutaneous fat was plentiful, but not of female distribution. The abdomen was still somewhat protuberant, but there were no palpable organs. A small area of the laparotomy incision was in the process of healing. The genitalia were those of a normal male child of 9 years. Examination of the eyes revealed nothing abnormal. The tonsils were slightly enlarged, but there were no lesions, hyperemia, or exudate. The patient had no complaints of any kind.

During a follow-up study six weeks later, the child appeared to be enjoying increasingly good health. The moon-shaped facies had disappeared. The abdominal incision had completely healed. The patient had recovered promptly from a tonsillectomy. Reactions to all tests were within normal limits.

Six months later, the child's physical, mental, and emotional development were normal. Two years later, at the time of this writing, he continues to be well.

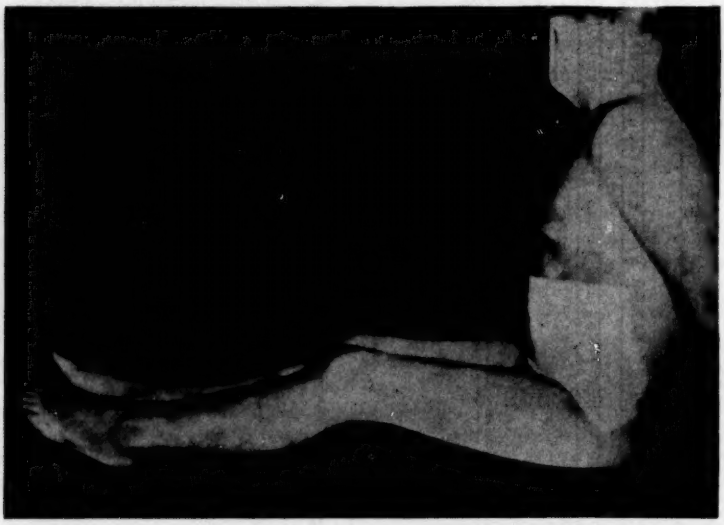

Fig. 4—By the 52d day of cortisone therapy, the muscles of the legs were rehabilitated, and the knees were almost completely straight. The patient had been able to walk since the second day of therapy, except during two exacerbations of brief duration. Although he had gained 18 lb. (30.8 kg.), there was no evidence of fluid retention. Note the moon-shaped facies.

COMMENT

Summarizing the literature on the etiology of periarteritis nodosa, Selye[11] recently observed: "Most of the monographs emphasize that rheumatic fever, allergies, infections, intoxications, and a variety of other stressors may act as eliciting agents. Allergic reactions to foreign sera, various micro-organisms, sulfonamides, etc., are particularly prone to produce periarteritis nodosa." He and his associates found that of all the vascular diseases, periarteritis nodosa was most

11. Selye, H.: The Physiology and Pathology of Exposure to Stress: A Treatise Based on the Concepts of the General-Adaptation-Syndrome and the Diseases of Adaptation, Montreal, Acta, Inc., 1950, p. 583.

accurately and most consistently reproduced in experimental animals by stress, lyophilized anterior pituitary tissue, mineralocorticoids, and renal pressor substance. It was one of the first maladies considered by his group to be a disease of adaptation.

The case reported here presented a history of what appeared to be allergic rhinitis, with a familial history of hay fever and asthma. Sulfonamide therapy had elicited allergic reactions prior to his being treated by us. Other stressors that may have produced, or prolonged the course of, periarteritis nodosa were not apparent in the history.

Cortisone and corticotropin (ACTH) have been used by other clinicians in the treatment of periarteritis nodosa in adults. Varying degrees of benefit from the administration of corticotropin have been reported by Goldman and co-workers,[12] Rosenberg,[13] Stillman,[14] Tucker,[15] Shick and co-workers,[16] and Carey and co-workers.[17] In most cases, however, relapse occurred, or deleterious effects were observed (such as hypertension or edema) which were attributed to the physiologic action of the drug. Somewhat better results were obtained by Shick [16] and by Carey [17] while administering cortisone to adults for this disease. However, complete recoveries were rare, and the mortality rate has been estimated as 95% among patients of all ages.

Studies of therapy for periarteritis nodosa in children appear less often in the literature than autopsy reports of young patients who have died of this disease.[18] However, methods of treatment have been proposed in a few reports. Goldman and co-workers [18] obtained apparent recovery in a 6-year-old child during the administration of sulfapyridine. Vining [19] reported apparent recovery in a 7-year-old child following symptomatic treatment without specific therapy. Coe and co-workers [20] recorded the case of a 9-year-old boy who died of periarteritis nodosa,

12. Goldman, R.; Adams, W. S.; Beck, W. S.; Levin, M.; Bassett, S. H., and White, A.: The Effects of ACTH on One Case of Periarteritis Nodosa, in Proceedings of the First Clinical ACTH Conference, edited by J. R. Mote, Philadelphia, Blakiston Company, 1950, p. 437.

13. Rosenberg, I. N.; Cleroux, A. P.; Raben, M. S.; Payne, R. W., and Astwood, E. B.: Clinical Evaluation of Corticotropin Therapy, A. M. A. Arch. Int. Med. **88**:211-234, 1951.

14. Stillman, J. S.: The Effects of ACTH on One Case of Periarteritis Nodosa: Discussion, in Proceedings of the First Clinical ACTH Conference, edited by J. R. Mote, Philadelphia, Blakiston Company, 1950, p. 445.

15. Tucker, H. St. G., Jr.; Taliaferro, I.; James, G., III, and Porter, W. B.: Observations on the Use of ACTH in Periarteritis Nodosa, in Proceedings of the Second Clinical ACTH Conference, edited by J. R. Mote, Philadelphia, Blakiston Company, 1951.

16. Shick, R. M.: Baggenstoss, A. H., and Polley, H. F.: The Effects of Cortisone and ACTH on Periarteritis Nodosa and Cranial Arteritis: Preliminary Report, Proc. Staff Meet., Mayo Clin. **25**:135, 1950.

17. Carey, R. A.; Harvey, A. M., and Howard, J. E.: The Effect of the Adrenocorticotropic Hormone (ACTH) and Cortisone on the Course of Disseminated Lupus Erythematosus and Periarteritis Nodosa, Bull. Johns Hopkins Hosp. **87**:425-460, 1950.

18. Goldman, B. A.; Dickens, K. L., and Schenken, J. R.: The Apparent Cure of Periarteritis Nodosa with Sulfapyridine: Report of a Case, Am. J. M. Sc. **204**:443-447, 1942.

19. Vining, C. W.: Periarteritis Nodosa: Case with Subcutaneous Lesions and Recovery, Arch. Dis. Childhood **13**:31-44, 1938.

20. Coe, M.; Reisman, H. A., and De Hoff, J.: Periarteritis Nodosa in a 9 Year Old Child, J. Pediat. **18**:793-798, 1941.

although treated with mercurials, digitalis, and supportive measures. Klein [8] treated a 7-year-old patient with sodium salicylate and supportive measures and observed apparent recovery in seven months.

Fager and co-workers [21] reported the death of a 4-month-old boy after treatment with penicillin, aureomycin, and supportive measures. Adelson [22] reported the autopsy of another 4-month-old boy who died after penicillin therapy. Branch and Roberts [10] reported the course of the disease in an 8-year-old boy who survived after treatment with penicillin, sulfadiazine, dihydrostreptomycin, aureomycin, anticoagulants, and supportive measures, but did not recover completely.

We believe it is significant that under therapy with cortisone and vitamins, after all other drugs had been withdrawn, recovery was progressive in our patient.

Cortisone together with multiple vitamins appeared to be a safe and effective treatment for periarteritis nodosa in this patient. Cortisone was used rather than corticotropin because of the ease with which it could be administered and because of the mild and transient nature of its side-effects in children. Although this substance was given continuously for 55 days, none of the untoward reactions listed by Derbes and Weiss [23] were present in the patient six weeks after cortisone therapy was withdrawn. During therapy, and for a brief period following its termination, mild Cushingoid features were observed, moon-shaped facies, and a slight euphoria. There was rapid weight gain, but no fluid retention. Healing of an abdominal incision was retarded, but a few weeks after use of cortisone was discontinued the patient recovered promptly from a tonsillectomy.

Cortisone given in large doses is apt to favor the dissemination of tuberculosis.[23] In the presence of a 4+ reaction to the intradermal tuberculin test in our patient, gastric washings and sputum were repeatedly cultured for tubercle bacilli, and repeatedly found negative, before cortisone therapy was initiated.

There is a possibility that prolonged use of cortisone in large doses may cause varying degrees of atrophy of the adrenal cortex. In most cases of adrenocortical atrophy attributed to cortisone, it is difficult to differentiate between the effect of the disease and the effect of the drug on the adrenal cortex. This patient showed no symptoms of adrenocortical atrophy at any time. Had such symptoms appeared after discontinuance of cortisone, we would have again placed the child on a minimum maintenance dose of 25 mg. per day and withdrawn the drug more gradually.

Selye cautions against the use of adrenal steroids for treating periarteritis nodosa in the presence of severe kidney damage. He states:

> Most patients treated with ACTH or cortisone for periarteritis nodosa, or the closely related cranial arteritis, respond very favorably. There is rapid improvement in their general condition, drop of fever and of the high erythrocyte sedimentation rate, as well as histologic evidence of healing in the vascular wall. However, occasionally this may be associated with an aggravation of their renal manifestations, especially in the presence of pre-existent severe kidney damage. Only exceptional patients fail to respond, and even this may be a matter of dosage.[24]

It did not appear that cortisone cured periarteritis nodosa in our patient. We could not even be certain that it shortened the course of the disease. The hormone

21. Fager, D. B.; Bigler, J. A., and Simonds, P.: Polyarteritis Nodosa in Infancy and Childhood, J. Pediat. **39**:65-79, 1951.

22. Adelson, L.: Periarteritis Nodosa in Infancy, J. Pediat. **39**:346-353, 1951.

23. Derbes, V. J., and Weiss, T. E.: Untoward Reactions of Cortisone and ACTH, Springfield, Charles C Thomas, Publisher, 1951, p. 28.

24. Selye, H.: Annual Report on Stress, Montreal, Acta, Inc., 1951, p. 344.

may have served only to suppress the local and systemic reactions to the condition that might otherwise have proved fatal, and thus provided protection for a period of time during which the processes abated.

SUMMARY

A case is reported of a 9-year-old boy who apparently recovered from periarteritis nodosa during a 55-day period of therapy with cortisone, vitamins, and acetylsalicylic acid. The hormone was administered after penicillin, streptomycin, aureomycin, sulfonamides, and other measures had proved ineffectual. The patient has been free of symptoms, and his physical, mental, and emotional development have now progressed normally for two years since withdrawal of the drug.

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CHRONIC GASTRIC ULCER IN CHILDHOOD

A Critical Analysis of the Literature with Report of a Case in an Eleven-Year-Old Boy

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CEDAR RAPIDS, IOWA

EVERY physician who cares for children in private practice knows there are few complaints he has to listen to more frequently than those of recurrent "tummyaches." We all are—or at least should be—reluctant to shrug off such complaints as being due to emotional disturbances, or to call them "functional" pains. Yet even after careful studies, organic causes are rarely found.

Should we x-ray every child with chronic abdominal complaints? Obviously, that would be impractical. However, one should not forget that the rare diseases do occur, and an 11-year-old boy recently seen in private practice proves this point.

REPORT OF CASE

This child had been complaining of "stomach-aches" for the past two years. He never vomited, and his mother volunteered the rather significant remark that "the stomach-aches were not any more frequent than most children have." During the preceding half year, he had complained of abdominal pains about twice a month. These attacks would last from 5 to 10 minutes and had no relation to food intake. His appetite had been very good. He had had physical check-ups twice a year and nothing unusual was ever found. Recently, he came from his home in Wisconsin to visit with his grandparents in Cedar Rapids. Shortly after arrival, he again complained of abdominal pain, this time accompanied by vomiting. A diagnosis of "stomach-flu" was made, and Pepto-Bismol (a preparation containing bismuth subsalicylate) was prescribed. Since the child continued to complain and vomit, his grandmother sought pediatric consultation. I saw the child at the home, which gave me an opportunity to inspect the material he had vomited. It was of dark brownish color. The boy's temperature was 99.4 F. He was a well-nourished husky-looking lad who appeared anything but chronically ill. The abdomen was soft, but there was moderate diffuse tenderness to palpation over the epigastrium. Since he had not had a bowel movement for over 48 hours, he was admitted to the hospital with a tentative diagnosis of intestinal obstruction. X-ray studies, however, failed to corroborate this impression. Because of the "coffee-ground" appearance of the vomitus, the possibility of peptic ulcer was then considered, although it was realized that this condition is very rare in children.

X-ray examination of the upper gastrointestinal tract resulted in the demonstration of a gastric ulcer on the lesser curvature, about 1 in. (2.5 cm.) from the pylorus, ¼ in. (0.7 cm.) in diameter, and about ¼ in. deep (Fig. 1). The emptying time of the stomach and the appearance of the duodenum were both normal. The first four days in the hospital were marked by the passage of a tarry formed stool and three episodes of hematemesis. The child complained of a good deal of upper abdominal pain, but the abdomen remained soft to palpation at all times. On the third hospital day, the boy was given 50 mg. of methantheline (Banthine) bromide every six hours. Forty-eight hours later all abdominal distress has ceased. The drug was continued throughout his hospital stay, and there was no more abdominal pain at any time. He was fed a Meulengracht diet, which he tolerated well, and he gained 1 lb. (0.5 kg.) in 15 days.

Laboratory studies revealed the following facts: urinalysis gave normal values; hemoglobin was 14.8 gm. per 100 cc. on admission (12 days later, 16 gm.); the red blood cell count was

From the Department of Pediatrics, Mercy Hospital.

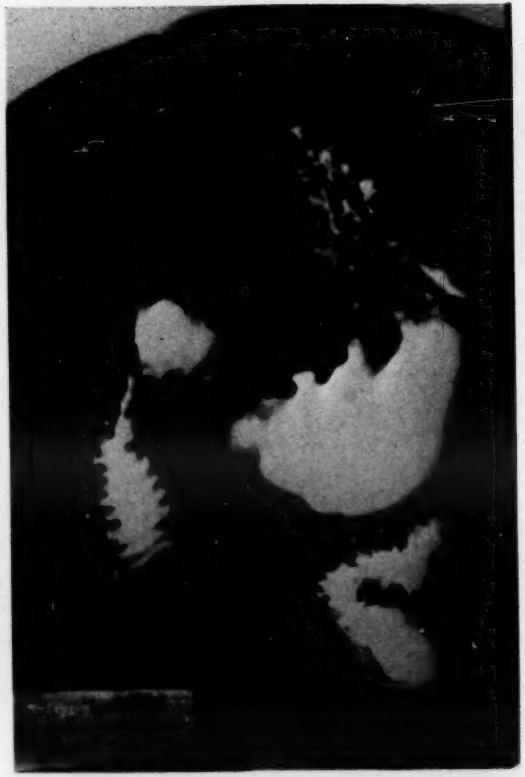

Fig. 1.—X-ray showing definite crater on lesser curvature.

Fig. 2.—X-ray taken one month after original film, showing complete healing of ulcer.

5,320,000 per cubic millimeter; the white blood cell count was 11,500 per cubic millimeter (12 days later, 8,050); the differential count was normal, and the platelet count was normal. One month after the diagnosis was made and two weeks after methantheline therapy was discontinued, a gastric analysis showed a total acidity of 11 degrees and no free HCl.

Eleven days after the original films were made, x-ray examination revealed a decrease in the size of the ulcer of approximately ⅛ in. (0.4 cm.). Follow-up films another two weeks later showed complete healing of the ulcer. X-ray films made in January, 1952, did not show any evidence of an ulcer, and the emptying time of the stomach was normal (Fig. 2).

COMMENT

To the average physician, the occurrence of a gastric ulcer in a child is practically unheard of, although duodenal ulcers in childhood are not too uncommon (Bird[1]). An analysis of the many publications dealing with peptic ulcers proved to be a major undertaking, mainly for three reasons: first, because many cases reported as gastric ulcers lack the necessary diagnostic proof; second, because a proper separation of gastric and duodenal ulcers often has not been made, and, finally, because of a conspicuous absence of strict criteria as to what constitutes a chronic gastric ulcer in children. The literature contains three attempts to clarify this point; I am referring to the papers by Thiele,[2] Proctor,[3] and Kennedy.[4]

Thiele, in Switzerland, recognized as early as 1919 the need for a proper classification of gastric ulcers in childhood. He published one of the most extensive papers on the subject, dividing ulcers in children into eight groups. These are (translated from the German):

1. Acute ulcerations in the newborn (melena)
2. Ulcers due to nutritional disturbances (ulcers of marantic infants)
3. Ulcers due to burns
4. Tuberculous ulcers
5. Ulcus syphiliticum
6. Secondary ulcers due to infection
7. Ulcers due to inflammatory or congestive changes of the mucous membranes
8. Ulcus chronicum simplex

Proctor defines an ulcer as "chronic" only "when symptoms or signs of its existence have been present for two months or longer, or when an ulcer . . . is calloused or indurated, with raised edges, or has sufficient adhesions to neighboring structures of a character which will leave little doubt that the process is chronic."

Kennedy divides ulcers into "several, distinct groups, according to age." His classification has been accepted by Ivy[5] in his remarkable book "Peptic Ulcer," one of the newest and most comprehensive works published on the subject. Three types of ulcers are recognized in infants and children: The first type is found in the newborn and frequently accounts for melena neonatorum; the second type occurs between the end of the first two weeks of life and the end of the first year; the

1. Bird, C. E.; Limper, M. A., and Mayer, J. M.: Ann. Surg. **114**:526, 1941.
2. Theile, P.: Ergebn. inn. Med. u. Kinderh. **16**:302, 1919.
3. Proctor, O. S.: Surg., Gynec. & Obst. **41**:63, 1925.
4. Kennedy, R. L. J.: Am. J. Dis. Child. **28**:694, 1924.
5. Ivy, A. C.; Grossman, M. I., and Bachrach, W. H.: Peptic Ulcer, Philadelphia, The Blakiston Company, 1950.

third type of ulcer is the chronic type, lacking the usual classic symptoms in patients less than 9 years old, but resembling the picture as seen in the adult in children over 9 years of age.

Many statistical data have been accumulated concerning the incidence of gastric ulcers in children, but, strangely enough, no report has appeared in over 25 years which would withstand a critical analysis. It is interesting to read in the older literature that even clinicians of wide experience have rarely seen a case of gastric ulcer in a child.

Lockwood [6] states that Koplik had seen but one case in his experience covering 300,000 cases of diseases in children. Rockitansky, famous European physician, never saw an ulcer in a child less than 14 years old. Cutler [7] tells us in 1904 that the Boston Children's Hospital, which opened its doors in July, 1869, has never had a case of gastric ulcer in a child, and that the Massachusetts General Hospital, which opened in September, 1821, has had but three cases in children less than 14 years old. In all three, however, the diagnosis was based on the occurrence of hematemesis only. Also, according to Cutler, "none of the members of the pediatric department in the Harvard Medical School have ever met with a case." Proctor gives statistics from the Mayo Clinic in 1925. Of 8,260 cases of peptic ulcers seen between 1906 and 1924, only two occurred in children, and only one of those was a gastric ulcer.

Enlarging on Proctor's and Kennedy's definitions, I believe the chronic gastric ulcer in childhood can be defined as follows:

1. It is a chronic ulcer of the stomach (as defined by Ivy [8]) occurring in children between the ages of 1 and 16 years.

2. There must be clinical or pathologic evidence that the ulcer has existed for more than one month.

3. One or more ulcerations may be present.

4. As long as the exact cause of gastric ulcers remains unknown, there must be no concomitant pathologic findings of any other type which may possibly have some bearing on the formation of the ulcer (such as infections, burns, or diseases of the central nervous system).

5. Only those cases in which diagnosis has been made by visualization of the ulcer on an x-ray film, by surgery, or at autopsy are acceptable. Clinical diagnoses alone can hardly be accepted, since they will not establish the exact location of the ulcer (gastric or duodenal).

The following explanatory remarks are added to further clarify this five-point definition:

1. The age limit has been set—by necessity arbitrarily—at 16 years, because most pediatricians care for children up to that age, and most chronic ulcers are of sufficiently long duration to make it likely that they actually originated at an earlier age.

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6. Lockwood, C. D.: Tr. West. S. A. **23**:255, 1913.

7. Cutler, E. G.: Boston M. & S. J. **151**:367, 1904.

8. "An ulcer is a circumscribed defect which extends through the muscularis mucosae. A chronic ulcer is characterized by an abundance of fibrous tissue in its margin and floor. A local eosinophilia is usually present."

2. The duration of one month is chosen because practically all acute ulcers have a history of less than one month.

3. It is a well-known pathologic observation that gastric ulcers in children frequently are multiple.

Items 4 and 5 are self-explanatory.

The clinical diagnosis of gastric ulcer is generally based on the occurrence of hematemesis, but just as "not all is asthma that wheezes"—to quote Chevalier Jackson—similarly, not every hematemesis is due to a gastric ulcer. This is born out by Cautley's[9] report in a published case of "gastric ulcer" in 1906. A study of the original paper makes it very likely that this particular child had so-called Banti's disease rather than an ulcer. The spleen was enlarged, and the child was anemic and vomited blood. Another example of an unproved case widely quoted in the literature for the past 44 years is the patient observed by Adler,[10] reported as a gastric ulcer, but diagnosed by clinical findings only. Adler himself stated he "thinks" the diagnosis is "justifyable" by symptoms and response to treatment; conclusive proof, however, is lacking. To further demonstrate the complexity of evaluating the many case reports of gastric ulcers, it seems advisable to show a few examples of why a critical analysis is indicated. One of the earliest case reports is that by Sidey[11] in 1835. Although the diagnosis was confirmed by autopsy, this 14-year-old boy had symptoms relating to the ulcer for only five days. Pleuritis and pericarditis also were found. This case, therefore, should be classified as one of acute ulcer, found in connection with other infections. Thiele, however, includes it in his table of true chronic ulcers. Another case, listed in the same table, is that of Scheuer.[12] Surprisingly enough, Thiele gives the location of this ulcer as "stomach" and groups the depth of the ulcer as "one" (explaining in a footnote that this indicates an ulcer involving the mucosa only). Yet the diagnosis was made by clinical observation only. No x-ray examination or surgery was done, and the patient recovered. Although Thiele's paper is one of the most comprehensive studies published up to that time (1919), it is not a complete survey. The author himself admits that, owing to wartime conditions, he was unable to secure some of the pertient literature from overseas. He also conceded that several of the tabulated cases lack the necessary proof to make the diagnosis certain.

There are many other inconsistencies in the literature. Apparently they are due to the author's acceptance of previously summarized series and failure to check the correctness of data by perusal of the original reports.

Welch,[13] for instance, mentions 33 cases of "open ulcers between the ages of one and 20 years," but fails to supply a breakdown according to age.

Ingram,[14] in one of the latest tabulations, includes one of the three cases reported by Toro, that of a child with a 4 + Wassermann reaction, but he did not include several proved cases published prior to the date of his report. His own patient's ulcer must be grouped under acute rather than chronic ulcers.

9. Cautley, E.: Soc. Study Dis. Child. **6**:225, 1906.
10. Adler, H.: Am. J. M. Sc. **133**:135, 1907.
11. Sidey, Edinburgh M. & S. J. **44**:258, 1835.
12. Scheuer, Allg. Wien. med. Zeitung **14**:336, 1869.
13. Welch, W. H.: Pepper's System of Medicine, 1885, Vol. 2, p. 480.
14. Ingram, M. D.: Am. J. Roentgenol. **64**:765, 1950.

Lockwood includes in his paper several "personal communications" which fail to give the duration or location of the ulcer. Only one of these reports, that of a 13-year-old boy operated on by Halstead, is accompanied by sufficient information to make it an acceptable case.

Rufz's [15] case has been included in nearly every collection of gastric ulcers to date (Thiele,[2] Foshee,[16] Proctor,[3] and Ingram [14]). However, the patient has had a long history of illness with intermittent fever and progressive enlargement of the abdomen. Her father had died of tuberculosis, and it is most likely that she had tuberculosis.

At times, research was complicated by incomplete bibliographies in some of the older literature. Hume, for instance, reported a case of gastric ulcer in a child which can not be verified, since the reference to his paper, quoted by Jacobi,[17] fails to give the year of publication, and it could not be found.

Another source of confusion resulting in duplications of one and the same case report, are references found in the literature to Barthez and Sanné, Rilliet and Barthez, and Barthez and Rilliet. The correct references to these authors can be found in the bibliography.[18]

Terminology also created some difficulties. Covey,[19] for example, published a paper entitled "A Case of Duodenal Ulcer in a Child." The x-ray findings, however, were "pyloric ulcer" and anatomically the pylorus is a part of the stomach, not the duodenum. It is admitted that often it is difficult to properly classify pyloric ulcers, as is demonstrated by one of the patients reported by Burdick.[20] Thiele believes it is impossible to group such ulcers and refers to the classification of Soupault, who calls these ulcers *juxtapylorisch*.

One of the greatest difficulties lies in the proper differentiation between acute and chronic ulcers. A child who has complained of symptoms suggestive of an ulcer for only a few days may have had a "dormant" asymptomatic ulcer for weeks, possibly months. A separate table, therefore, has been prepared, listing children with ulcers of questionable duration, including especially those which have perforated, but which did not cause pain until time of perforation. Those which are probably acute ulcers also are included. No claim is laid to completeness of this list, since it is not the purpose of this study to analyze acute ulcers (Table 1).

We cannot see any advantage in recapitulating what has been said about the cause of gastric ulcers. Theories are many, but the exact cause remains obscure. As coincidence would have it, there is an article on peptic ulcers directly following Jacobi's paper on ulcers in children. It opens with the following remark: "It is

15. Rufz, E.: Gaz. méd. Paris **11**:673, 1843.

16. Foshee, J. C.: J. A. M. A. **99**:1336, 1932.

17. Jacobi, A.: New York M. J. **90**:837-840, 1909.

18. Barthez, E., and Traité clinique et practique des maladies des enfants, Ed. 2, Paris, J. B. Baillière et fils, 1853, Vol. 1, p. 797. Barthez, E., and Rilliet, F.: Handbuch der Kinderkrankheiten, translated by G. Krupp, Ed. 2, Leipzig, C. E. Kollmann, 1855, Vol. 1, p. 881. Rilliet, F., and Barthez, E.: Traité clinque et practique des maladies des enfants, Ed. 3, revised and with additions by E. Barthez and A. Sanne, Paris, J. B. Baillière et fils, 1887, Vol. 2, p. 365.

19. Covey, G. W.: Nebraska M. J. **5**:104, 1920.

20. Burdick, W. F.: J. Pediat. **17**:654, 1940.

impractical to analyze all the excellent experimental work and ingenious speculations on the pathogenesis of peptic ulcers." Thus stated already in 1909! One of the most recent enumerations of theories concerning the pathogenesis of ulcers can be found in a paper by Morgan.[21]

Concerning the diagnosis of gastric ulcers in children it has been stated many times that it is very difficult to recognize them, because signs and symptoms "are so diversified as to rob them of pathognomonic significance" (Kennedy). The clinical picture admittedly is quite different from that observed in adults. The classic symptoms of what Cecil calls "the rhythm of gastric ulcer" (food—comfort—pain —comfort—) are conspicuously absent in children.

Jankelson,[22] reporting two cases of gastric ulcers in 1932, emphasizes that the diagnosis is not sufficiently often made because (1) the diagnosis is not suspected; (2) in young children a proper history cannot be obtained; (3) there are no typical symptoms, and (4) x-ray studies are not made as commonly as in adults.

TABLE 1.—*Acute Gastric Ulcers and Ulcers of Questionable Duration*

Author	Age, Yr.	Sex	Duration	Method of Diagnosis*	Reference
Colgan	2½	F	Sudden	A	Med. News Philadelphia **61**:408, 1892
Parkinson	2	M	1 day	A	Rep. Soc. Study Dis. Child. **1**:143, 1901
Barker	10	M	4 days	A	Brooklyn M. J. **16**:519, 1902
Cheyne and Wilbe	13	M	1 day	S	Lancet **1**:1641, 1904
Stowell [23]	8	F	1 mo.	A	.....
Paterson	12	M	12 days	S	Scot. M. & S. J. **19**:228, 1906
Dietrich	7	M	Less than 1 mo.	A	Münch. med. Wchnschr. **59**:1, 638, 1912
Loeber	8	F	1 wk.	X	Arch. Pediat. **46**:578, 1929
Shore	1 10/12	F	"Acute"	A	Ann. Surg. **92**:234, 1930
Martin	6½	M	"Few days"	X	Radiology **55**:728, 1950
Motsay and Allen	2	M	1 mo.	X	Guthrie Clin. Bull. **19**:191, 1950
Ingram [14]	11	M	"36 hr."	X	.....
Gillespie and Bliss	2	M	Less than 1 mo.	S	Arch. Pediat. **68**:361, 1951

* A indicates autopsy; S, surgery, and X, x-ray examination.

Early diagnosis is, of course, most desirable, because recovery can be expected in most instances with early and adequate conservative treatment.

Greater accuracy in diagnosis could be achieved if x-ray studies would be instituted more frequently than has been done in the past. Most children with chronic ulcers give a sufficiently long history of abdominal distress to arouse the suspicion of organic disease. If an ulcer is not found during the first examination but symptoms persist, the child probably should be x-rayed again at a future date.

After a search of the world literature, as complete as we believe it is possible to make, and after elimination of all doubtful reports, there remain 39 cases of proved chronic gastric ulcers in children between the ages of 1 and 16 years which fulfill the criteria postulated above (Table 2). Including the case reported in this paper, this would make a total of 40 cases in over 100 years—a rare incidence indeed. For a matter of completeness, it should be emphasized that a perusal of the litera-

21. Morgan, R. H.: Am. J. M. Sc. **222**:590, 1951.
22. Jankelson, I. R.: Am. J. Dis. Child. **44**:162, 1932

ture reveals another 28 cases which must be classified as "probable but not proved chronic gastric ulcers." This does not include cases of children who were found to have ulcers but also had some other disease at the same time.

It is debatable whether some of these cases in which other pathologic processes were found besides the ulcer should not rightly be included in the series of cases of

TABLE 2.—*Cases of Proved Chronic Gastric Ulcer in Childhood, Conforming to Criteria Set Forth in Text*

Author and Yr. Reported	Age, Yr.	Sex	Duration of Symptoms	Method of Diagnosis*	Reference
Buzzard, 1861	9	F	Sudden onset†	A	Tr. Path. Soc. London **12**:84, 1861
Verliac, 1865	14	M	2 yr.	S	Bull. Soc. anat. Paris, 1865
Reimer, 1869	3½	F	2½ yr.	A	Jahrb. Kinderh. **10**:291, 1876
Keays, 1903	16	F	1 yr.	A	Brit. M. J. **2**:1459, 1903
Bechthold, 1904	5	..	5 mo.	A	Jahrb. Kinderh. **60**:347, 1904
Reichelt, 1905	8	M	1 yr.	A	Wien. med. Presse **46**:126, 1905
Robinson, 1905	14	M	1 yr.	A	Internat. Clin. **3**:119, 1905
v. Eiselsberg, 1905	12	F	1 yr.	A	See Stowell [23]
Lund, 1909	8	F	1 yr.	S	Boston M. & S. J. **161**:930, 1909
v. Cackovic, 1912	14	M	7 yr.	S	Arch. klin. Chir. **98**:301, 1912
	13	F	2 yr.	S	
Halstead, 1913	11	..	4 yr.	S	Personal communication to Lockwood
Lockwood, 1913 [6]	13	..	1½ yr.	S	.....
Gordon, 1919	12	F	9 yr.	S	Long Island M. J. **13**:132, 1919
Thiele, 1919 [2]	13	F	4 mo.	A	.....
Sanjek, 1920	12	F	1 yr.	S	Zentralbl. ges. Chir. **9**:314, 1920
Proctor, 1923 [3]	14	M	6 yr.	X&S	.....
Norrlin, 1923	7	F	3 yr.	S	Acta chir. scandinav. **56**:309, 1923/24
Weber, 1925	12	M	4 yr.	S	Arch. klin. Chir. **137**:731, 1925
	15	M	4 yr.	S	
Paus, 1926	9	M	3 yr.	S	Acta chir. scandinav. **61**:40, 1927
	14	M	10 yr.	S	
Ogelvie, 1927	14	F	1¼ yr.	A	Newcastle M. J. **8**:104, 1927-1928
Robinson, 1927	12	M	3 mo.	S	Lancet **2**:600, 1927
Nordentoft, 1927	13	M	2 days†	S	Acta chir. scandinav. **62**:426, 1927
Jankelson, 1932 [22]	12	F	7 mo.	X	.....
	12	M	5 mo.	X	
Holm, 1929	15	M	6 mo.	S	Ugesk. laeger **91**:649, 1929
Oldfield, 1932	13	M	2 yr.	X	Brit. M. J. **1**:836, 1932
Micheli, 1934	12	M	4 yr.	X&S	Boll. Soc. piedmont. chir. **4**:467, 1934
	13	F	1 yr.	X&S	
Olper, 1933	11	M	1 yr.	X&S	Arch. ital. mal. app. diger. **2**:39, 1933
Rocher, 1934	8	M	4 yr.	X&S	Rev. franc. pediat. **10**:218, 1934
Toro, 1937	11	M	1 yr.	X&S	Pediatria **45**:904, 1937
Bertrand, 1937	12	F	2 yr.	X&S	Arch. argent. pediat. **8**:990, 1937
Colson, 1938	15	M	Few hr.†	S	Lyon méd. **162**:35, 1938
Burdick, 1940 [20]	10	F	"Several" yr.	X	.....
Logan and others, 1941	12	F	1 yr.	X&S	Ann. Surg. **113**:260, 1941
Kraemer and others 1942	6	M	1 yr.	X	Am. J. Digest Dis. **9**:338, 1942

* A indicates autopsy; S, surgery, and X, x-ray.
† Ulcer found to be indurated.

true ulcers. I refer specifically to the report by Guntz cited by Stowell,[23] in which he described a gastric ulcer in a child who also had scarlet fever and to one of the four children in the cases reported by Fenwick,[24] as well as Francine's [25] case,

23. Stowell, W. L.: M. Rec. **68**:52, 1905.

24. Fenwick, cited by Stowell, W. L.: M. Rec. **68**:52, 1905.

25. Francine, A. P.: Am. J. M. Sc. **129**:429, 1905.

in which pneumonia was a concomitant disease. I believe it is agreed that neither scarlet fever nor pneumonia is likely to have any connection with the formation of a gastric ulcer. However, to secure an intelligent evaluation of case reports, it seemed imperative to set down and adhere to some definite criteria; separate classification of such cases, as has been done—although not consistently—by Thiele, is the logical compromise.

SUMMARY

A case of chronic gastric ulcer in an 11-year-old boy is described. The diagnosis was made by x-ray examination following an episode of hematemesis. The child made an uneventful recovery. The literature on the subject to date has been analyzed, leaving 39 cases of true chronic gastric ulcers. There are many other instances of gastric ulcers reported in the literature; the diagnosis, however, was based on clinical observation only and could not be confirmed.

GALACTOSEMIA

An Unusual Cause of Neonatal Jaundice

DONALD JOHNS, M.D.
GRAND RAPIDS, MICH.

CHRONIC galactosemia, or galactose diabetes, is a disorder of carbohydrate metabolism in which there seems to be an inability of the liver to convert galactose into glycogen satisfactorily. The metabolic error may be a decreased conversion of galactose into glucose, most likely an enzymatic want or defect.[1] This disease, one of the so-called inborn errors of metabolism, though rare, is being reported more frequently in the current pediatric literature. Bell and co-workers [2] in 1950 reviewed 15 cases reported in the literature prior to their study of 2 cases, and in the ensuing two years an almost equal number of cases have come to light.

The purpose of this paper, in addition to adding three more cases (all in one family), is to illustrate and emphasize that icterus may be a primary and not a secondary feature of the disease and to reemphasize the importance of early diagnosis, since it is well known that any or all of the severe toxic manifestations of this disease are reversible if the anomaly is detected early in life. In hardly any other metabolic disorder can such gratifying results be attained as occur in this entity simply by the elimination from the diet of galactose, a nonessential food substance present only in milk and milk-containing foods. This is easily accomplished by the use of any well-known milk substitute.

In addition, it is hoped that this paper may further stimulate closer scrutiny of the records of infants who died in early life of "idiopathic cirrhosis of the liver" in the hope that on siblings born subsequently there may be more definite diagnostic studies done along this line, since it is well known that this disorder may be hereditary. Conceivably, many infants dead of hepatic cirrhosis early in life may have had this metabolic disorder. Any infant who has cirrhosis of the liver, therefore, should have the benefit of the simple studies necessary to diagnose galactosemia.

Excellent reviews of the literature are presented elsewhere.[2] The essential features of this entity are hepatomegaly, with or without splenomegaly, melituria (specifically galactosuria), albuminuria, and severe malnutrition. Mental retardation, lamellar cataracts, and icterus accompany these and are related to the severity of the disease. Other features may include anemia, osteoporosis, lethargy, and absence of the tendon and Moro reflexes.

The cases being reported are interesting in that all three of the children in one family presented the diagnostic problems of neonatal jaundice. Each infant became icteric starting on the fourth day of life. The first two infants died with the

From the Department of Pediatrics, Butterworth Hospital.

1. Falls, H. F.; Lowrey, G. H., and Anderson, W. C.: Galactosemia Cataract: Report of a Case, Am. J. Ophth. **34**:1271, 1951.

2. Bell, L. S.; Blair, W. C.; Lindsay, S., and Watson, S. J.: Galactose Diabetes (Galactosemia): Clinicopathologic Study of 2 Siblings, J. Pediat. **36**:427, 1950.

diagnosis undetermined, but the lastborn is still living and quite well, having passed his first birthday. It seems highly probable that this retrospective diagnosis is correct for the first two in light of the similar clinical picture and conclusive studies found with the lastborn.

REPORT OF CASES

CASE 1.—J. D. was the first of three sons born of healthy white parents; birth occurred in August, 1945. The pregnancy was uncomplicated, labor was of approximately 15 hours' duration,

Fig. 1.—Section of the liver; low magnification. Marked cirrhosis with only irregular islands of liver parenchyma preserved.

and the delivery was normal. The infant weighed 8 lb. 6 oz. (3,800 gm.) at birth and cried vigorously. He was fed evaporated-milk formula, and except for a left clubbed-foot deformity seemed perfectly well. When he was 4 days of age, the parents noticed that he was becoming jaundiced, and he also began to vomit most of his feedings.

The father was 24 years old and the mother 22 years old. Both were healthy, and there was no history of any familial or hereditary disease. The baby's blood was Type A, Rh

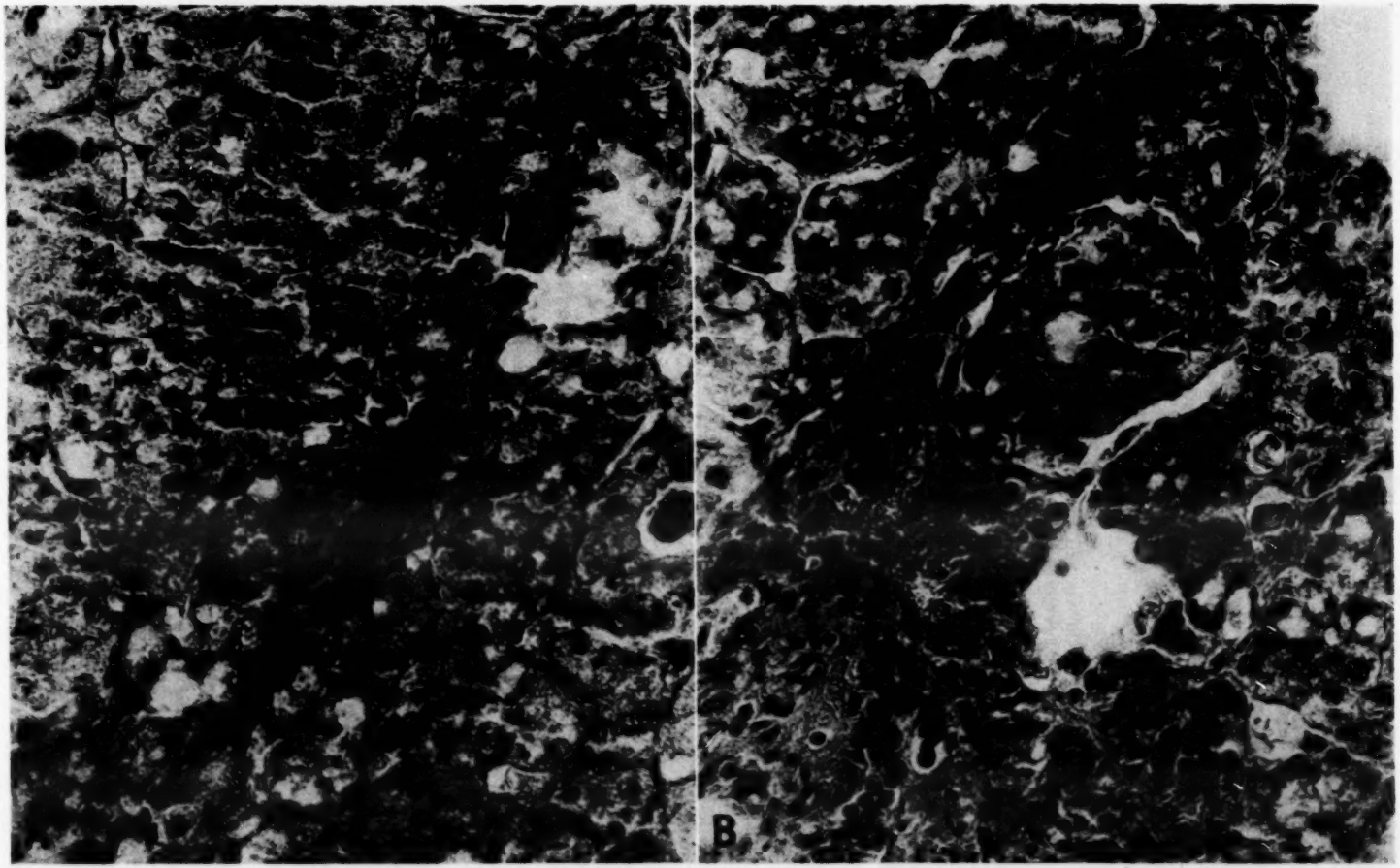


Fig. 2.—Same as Figure 1; high magnification. *A*, the liver parenchyma consists of large cells with granular cytoplasm and some large fat droplets. The bile canaliculi are filled with inspissated bile. *B*, note alveolar grouping of liver cells characteristic of this disease.

positive. The Kahn test was negative. The mother and father had negative Kahn reactions and were Rh positive. The mother had Type A blood. The baby's blood cell count was essentially normal, but no other laboratory data are available.

After the jaundice and vomiting appeared, the abdomen began to enlarge rapidly. The evaporated milk formula was still used, but the infant's appetite became very poor. The jaundice, vomiting, and abdominal enlargement grew progressively worse, and he died suddenly at the age of 7 days. No autopsy was performed. The parents were told he had "liver jaundice."

CASE 2.—D. D., the second son, was admitted to Butterworth Hospital on May 21, 1947, at the age of 6 weeks, with the complaints of jaundice, vomiting, and enlargement of the abdomen.

He was delivered spontaneously after a full-term uneventful pregnancy. The birth weight was 8 lb. (3,630 gm.). He was well until a few days after birth, when he began to vomit his feedings of a standard evaporated-milk formula. At 4 days of age jaundice appeared, and after a few weeks this became severe, and the abdomen began to enlarge rapidly. The stools became very loose and green, and he lost weight rapidly. When his condition grew progressively worse he was sent to this hospital.

Physical examination revealed an acutely ill icteric infant with marked abdominal distention and dehydration. His weight on admission was 9 lb. (4,080 gm.) The liver edge was not felt. The heart and lungs were normal, and no other abnormalities were found.

The hemoglobin value was 9.8 gm. per 100 cc.; the red blood cell count was 3,410,000, and the white blood cell count was 16,200, with 74% polymorphonuclear leucocytes and 26% lymphocytes. The admission urine specimen showed a 1+ reaction for sugar, a trace of albumin, and a moderate amount of granular casts. The icteric index was 20. The Kahn test was negative; the baby's blood was Type A, Rh positive. The prothrombin time was 75% of normal.

On admission a paracentesis was performed, and approximately 380 cc. of clear yellow fluid was withdrawn from the peritoneal cavity. Studies of the sediment, including routine and acid-fast cultures, were negative. After aspiration of the ascitic fluid, the liver edge was easily felt below the right costal margin. The baby was fed an evaporated-milk formula while in the hospital, but continued to vomit all feedings. Urinalysis again showed a trace of reducing substance, with albuminuria and granular casts as well. The icteric index remained elevated (26), and the direct van den Bergh reaction was positive.

The baby lost weight slowly; the hemoglobin value and the red blood cell count dropped precipitously. He was given penicillin, whole blood transfusions, multivitamins, and liver extract. On June 13, 1947, at the age of 7 weeks, an exploratory laparotomy was done, and the surgeon reported, "No evidence of portal obstruction was seen, but the liver was very firm and enlarged." A biopsy of the right lobe of the liver was done and this was interpreted as showing "early cirrhosis of the liver with much fatty infiltration suggesting liver damage" (Figs. 1 and 2).

After the surgery his condition grew critical, and within 24 hours twitchings and generalized convulsions developed, and he died. No autopsy was done.

CASE 3.—S. D., the third son, was admitted to the pediatric service of Butterworth Hospital in Aug. 3, 1951, at the age of 12 days, with the complaint of jaundice of seven days' duration. He had also been vomiting, and his abdomen was enlarged.

The baby was born at term on July 23, 1951, after an uncomplicated pregnancy. Birth occurred after a four-hour labor; delivery was spontaneous and the birth weight was 8 lb. 6 oz.

This baby, like the first, had a left clubbed-foot deformity, but apart from this seemed to be perfectly normal. A cast was applied to the foot, and he was discharged from the hospital with his mother on the fifth day. An evaporated-milk formula was given to him, but on the fourth day he began to vomit a little and was mildly jaundiced. The vomiting quickly became projectile, and the jaundice deepened. No loss of appetite was noted, however. When his abdomen began to enlarge, and the other symptoms persisted, he was sent to the hospital.

His temperature on admission was 99 F. Examination revealed an acutely ill dehydrated infant with a moderate amount of jaundice. The liver edge was firm and extended approximately 5 cm. below the right costal margin. The lungs and heart were normal. There was a talipes equinovarus deformity of the left foot. No tendon reflexes could be elicited; the baby was very lethargic, and the Moro reflex was absent.

The urine constantly showed a 1 to 3+ reaction for sugar, 2 to 3+ reaction for albumin, and granular casts. No acetone was found, but urobilinogen was present. The hemoglobin value was 15.4 gm. per 100 cc.; the red blood cell count was 4,860,000, and the white blood cell count was 10,200, with a differential count of 36% polymorphonuclear leucocytes and 64% lymphocytes. The Kahn reaction was negative, and the blood was Type A, Rh positive. The nonprotein nitrogen was 25 mg. per 100 cc., the cephalin flocculation was 3+, and the prothrombin time was 100%. Roentgenograms of the chest and long bones showed no significant abnormalities.

On admission the evaporated-milk formula was continued, but this was taken poorly, and the vomiting persisted. The patient remained lethargic, cried little, and did not move spontaneously. The jaundice did not change.

Because two siblings had died shortly after birth under exactly similar circumstances, a hereditary metabolic defect was thought of, and when melituria was discovered a 24-hour specimen of urine was analyzed. Fermentation tests were done, and the reducing substance was found to be nonfermentable. The mucic acid test was positive, indicating the presence of galactose or lactose. An osazone crystal isolated by the phenylhydrazine method proved to be the galactose crystal.

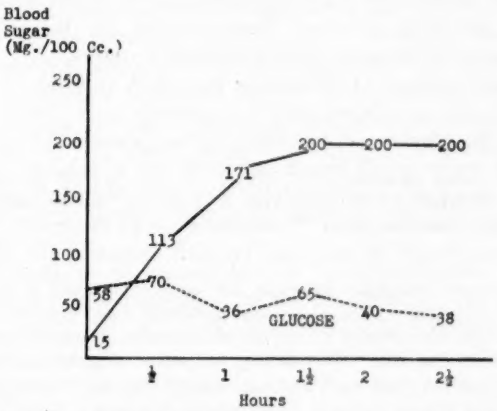


Fig. 3 (Case 3).—Oral galactose-tolerance curves. Note the prolonged high curve of blood galactose, with the depressed glucose levels.

At this time bilateral lamellar cataracts were easily seen, and the condition of the patient became critical. His hemoglobin value dropped to 9.8 gm. per 100 cc., with a red blood cell count of only 3,200,000. Therefore, further diagnostic tests were deferred temporarily, two blood transfusions were given, and the formula was changed to Nutramigen.[3] Within 24 hours reducing substance was no longer found in the urine, and the albuminuria disappeared in three days. The baby took the new formula well, and the vomiting ceased almost at once. He started to gain weight immediately, rapidly at first and more slowly later. Within a week the tendon and Moro reflexes began to appear, and they became normal in a short time. With this he became more alert, moved spontaneously, and began to cry vigorously.

When his condition improved, an oral galactose-tolerance test (1.75 gm. per kilogram of body weight) was done, and this exhibited the typical curve seen with this disease: a high prolonged level of nonfermentable reducing substance (galactose) accompanied by a simultaneous fall in the fermentable portion (glucose) as shown in Figure 3.

From this point on, the picture was that of continued rapid improvement. During the second month the liver had decreased markedly in size, the spleen was no longer palpable, the jaundice

3. Nutramigen is a lactose-free milk containing hydrolyzed casein with balanced amounts of carbohydrate, fat, and minerals.

had disappeared entirely, and repeated urinalyses and blood cell counts were normal. He was fed Nutramigen and multivitamin and iron concentrate preparations. Follow-up visits thereafter revealed the disappearance of the cataracts and hepatomegaly by the age of 3½ months, and his mental and physical development was progressing in a very normal fashion. On March 15, 1952, the cephalin flocculation test was negative, and the prothrombin time was 95% of normal. The nonprotein nitrogen was 41 mg. per 100 cc., and the blood cell counts and urinalyses were normal. At this time, after having passed his first birthday, he is on a regular diet with the exception of having Nutramigen instead of milk, and is allowed no milk-containing foods. The clubbed-foot deformity has responded to orthopedic treatment, and he is perfectly well in all respects.

COMMENT

These cases interestingly presented themselves as problems of jaundice in the early neonatal period. It would seem probable that the first two infants had galactosemia. In the lastborn infant, a carefully examined urine specimen was the clue to the ultimate diagnosis, since melituria is an important feature of the disease. It should be stated that if vomiting is severe, as it often is, only traces of reducing substance may be found in the urine, since there is a decreased amount of galactose-containing food ultimately absorbed. Demonstration that the reducing substance was nonfermentable led to more definite diagnostic studies.

The toxic manifestations of this disease have been ascribed to the high level of blood galactose,[4] and in support of this hypothesis it is stated that a strongly positive cephalin flocculation test demonstrates the presence of degenerative changes in the liver. The proteinuria is also thought to be due to renal damage by galactose. Galactose when given in excess to chicks produced death in convulsions, leading Dam[5] to postulate that the sugar is directly toxic to the brain. On the basis of their observations though, Mason and Turner[6] suggested the following theory:

> Since the body cannot metabolize galactose, this sugar accumulates in the blood and causes a depression of blood glucose. The high blood galactose level "deceives" the regulators of blood sugar and causes an excessive conversion of glucose to glycogen, which causes hepatomegaly and hepatic dysfunction. When lactose, the source of galactose, is withdrawn from the diet, normal glycogen-glucose equilibrium is re-established and the liver returns to normal. The low level of blood glucose results in tissue damage, presumably to the liver and kidney.

The validity of this theory has been questioned on the grounds that (1) surprisingly little liver disturbance occurs in glycogen-storage disease, in which excessive and extreme storage of glycogen in the liver is known to occur, (2) ordinarily the deposition of glycogen in the liver tends to protect the liver, and (3) hypoglycemia from other causes appears not to damage the liver or the kidneys.

The absence of the Moro reflex, the loss of tendon reflexes, and the lethargy all indicated central nervous system involvement; the albuminuria, the urinary casts, and the elevated blood nonprotein nitrogen reflected kidney damage; the icterus, hepatomegaly, and positive cephalin flocculation tests revealed liver pathology. Thus we readily see the widespread neurotoxic, nephrotoxic, and hepatotoxic effects of galactosemia. In a case studied by me and reported elsewhere in the literature[7] it was demonstrated that within a period of three to five days of

4. Mellinkoff, S.; Roth, B., and MacLaggan, J.: Galactosemia with Hepatic Damage: Report of Case in Infant with Recovery, J. Pediat. **27**:338, 1945.

5. Dam, H.: Galactose Poisoning in Chicks, Proc. Soc. Exper. Biol. & Med. **55**:55, 1944.

6. Mason, H. H., and Turner, M. E.: Chronic Galactemia: Report of Case with Studies on Carbohydrates, Am. J. Dis. Child. **50**:359, 1935.

7. Langewisch, W. H., and Bigler, J. A.: Disorders of Glycogen Metabolism: With Special Reference to Glycogen Storage Disease and Galactosemia, Pediatrics **9**:263, 1952.

milk (i. e., galactose) feedings, after being maintained for several days on a milk-free diet, albuminuria, prolonged prothrombin time, positive cephalin flocculation tests, elevated nonprotein nitrogen, lethargy, and disappearance of the tendon reflexes were observed. Reducing substance appeared in the urine within a day following resumption of milk feedings.

An analysis of the reported cases shows albuminuria, as well as melituria, as a constant finding, and this may at times be confusing in that a primary disease of the kidney may be suspected. It seems fairly certain that toxic depression of kidney function due to parenchymal damage by the abnormally high level of galactose in the blood would account for this and the accompanying azotemia. Anemia also seems to be a fairly uniform characteristic of the disease, due probably to toxic depression of normal marrow erythropoiesis.

Blood sugar levels are high in this disease, with the greater part being non-fermentable (galactose). Galactose-tolerance tests readily demonstrate a prolonged high curve of galactose and a reciprocal fall in the glucose level.[8]

Nearly half of the patients in the reported cases had either nuclear or zonular lenticular cataracts. The opacities may partially or completely disappear provided treatment is begun early before irreversible changes occur. Kirby and co-workers [9] demonstrated that galactose is directly toxic to lens tissue. Bellows and Chinn [10] suggested that galactose cataract is caused by the disturbances connected with the hyperglycemia and the resultant increased sugar content of the aqueous humor.

Together with all the other organ-system improvement, mental retardation can be largely or completely dissipated by early diagnosis and the prompt elimination of galactose from the diet.

Bell and co-workers [2] postulated that fat infiltration, rather than abnormal deposits of glycogen, is the basic cause of the abnormal size and function of the liver. The biopsy studies in Case 2 revealed extensive fat infiltration, together with early cirrhotic changes in the liver parenchyma, and these pathologic changes have been demonstrated by others.[11] These changes appear to be reversible.

SUMMARY

Three successive cases of galactosemia in one family are reported.

These cases were featured by neonatal jaundice.

The procedures for diagnosis and the symptomatology, clinical findings, treatment, and prognosis are discussed.

Early diagnosis for the prevention of permanent damage is emphasized.

Mrs. Mary Jane Eldred, M.T., assisted in the laboratory studies.

8. Bruck, E., and Rappoport, S.: Galactosemia in an Infant with Cataracts: Clinical Observations and Carbohydrate Studies, Am. J. Dis. Child. **70**:267, 1945.

9. Kirby, D. B.; Estey, K., and von Wiener, R. E.: A Study of the Effect of Changes in the Nutrient Medium on Lens Epithelium: Cultivated in Vitro, Tr. Am. Acad. Ophth. **37**:196, 1932.

10. Bellows, J. G., and Chinn, H.: Biochemistry of Lens: Production of Lens Opacities by Injection of Hypertonic Solutions, Arch. Ophth. **25**:796, 1941.

11. Mellinkoff, Roth, and Mac Laggen.[4] Townsend, E. H., Jr.; Mason, H. H., and Strong, P. S.: Galactosemia and Its Relation to Laennec's Cirrhosis: Review of the Literature and Presentation of 6 Additional Cases, Pediatrics **7**:760, 1951.

Obituaries

SAMUEL WOLCOTT CLAUSEN, M.D.

1888-1952

Samuel Wolcott Clausen was born in Canaseraga, N. Y., on Oct. 17, 1888, and died in Rochester, N. Y., Dec. 29, 1952.

Dr. Clausen was a graduate of Williams College (1910) and of the Johns Hopkins University School of Medicine (1915). After an internship in the Harriet Lane Home and a year in the chemical laboratory in internal medicine, he went with Dr. McKim Marriott to St. Louis, where he remained until 1924, when he became the first professor of pediatrics in the University of Rochester School of Medicine and Dentistry. Because of poor health he resigned on June 30, 1952. He was admitted to the American Pediatric Society in 1924, subsequently serving as a member of its Council and as Vice-President.

Other societies in which he took an active part were as follows: the American Chemical Society, the American Society for the Advancement of Science, the American Academy of Pediatrics, the Society for Experimental Biology and Medicine, and the Society for Pediatric Research.

As an investigator, teacher, and scholar he was admired by everyone who had the good fortune to be associated with him. Possessed of an unusual knowledge of mathematics and chemistry and a broad clinical experience, he became one of the truly great teachers of his time. His approach to a problem was logical and his conclusions accurate. His kind and sympathetic manner with patients and their relatives greatly impressed the younger members of his staff. One of his most cherished honors was that of the first Alumni Award in 1952 from his former students in the University of Rochester.

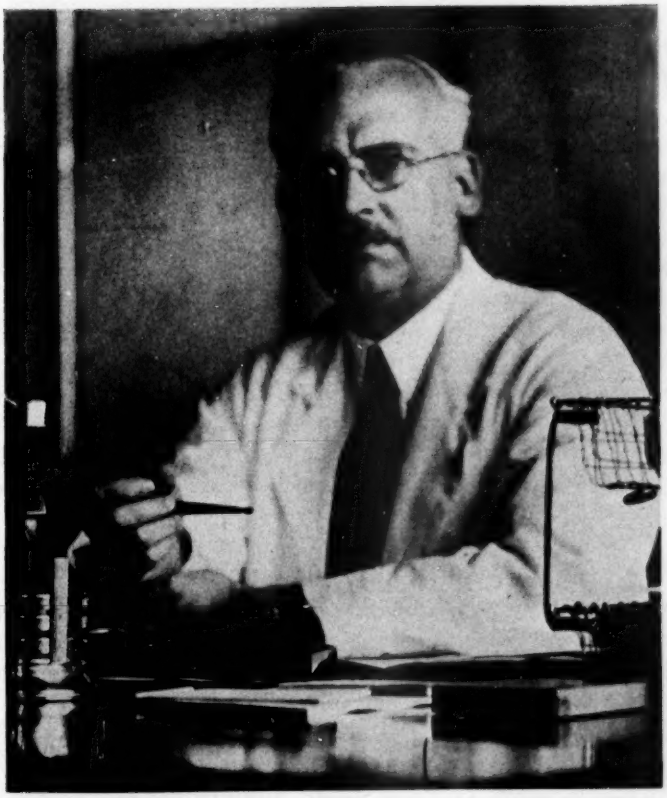
In the conduct of the department Dr. Clausen never directed the program of an associate, but remained always ready with able assistance and wise counsel when it was sought.

His own investigations concerned many complex problems, chiefly related to renal disease, nutrition, and vitamin A. In 1943 he gave a Harvey Lecture on "The Absorption and Storage of Vitamin A."

Dr. Clausen loved the outdoors, spending many of his vacations in travel abroad, in Canada, and in the western part of the United States. He enjoyed camping out. He spent many hours on his farm near Pittsford, N. Y., where he enjoyed gardening and the cultivation of flowers.

In 1927 he married Ethel Marjorie Luce, also a distinguished pediatrician and investigator, who survives him. They had no children.

With his death American pediatrics loses one of its finest figures: scholar, investigator, clinician, and teacher extraordinary.



SAMUEL WOLCOTT CLAUSEN, M.D.
1888-1952

LAWRENCE THOMAS ROYSTER, M.D.

1874-1953

Lawrence Thomas Royster, pioneer pediatrician, writer, and educator, died at his home in Charlottesville, Va., on Jan. 7, 1953.

Dr. Royster was born in Norfolk, Va., on Aug. 18, 1874. He was educated at Norfolk Academy and at the University of Virginia, from which he received an M.D. degree in 1897. He received formal postgraduate training in New York and later obtained additional training at Boston, Baltimore, and New York.

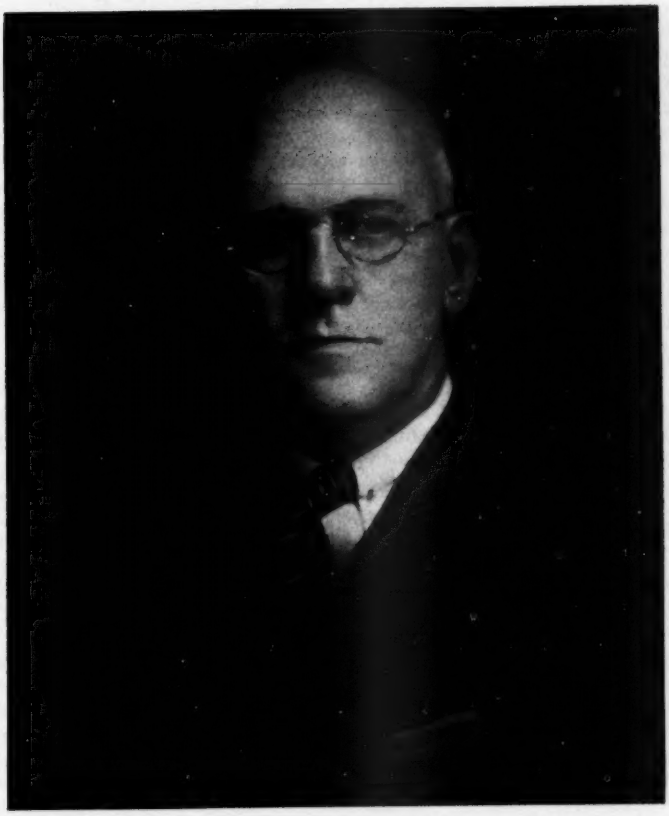
His early medical experience was in general medical practice in Norfolk, but after a few years he became interested in child welfare work and founded the first Society for the Prevention of Cruelty to Children in that area. From this interest he began to devote more of his energies to disease and social conditions in infants and children and was among the first medical men in the South to limit his practice to pediatrics. He became well known in his community and state, and, because of his outstanding interest in growth, development, and nutrition in children, his work began to appear in medical journals and books such as Appleton's "Pediatric Series," and Abt's "Pediatrics." He was co-author of the textbook "Pediatrics" with Dr. H. D. Chapin.

In 1923, because of his great pioneer work in the field of child health, he was asked by his alma mater to return and found the department of pediatrics in the department of medicine. Here his genius as a teacher and clinician served him well. In a few short years, his students and residents were becoming well known in Virginia as outstanding "baby doctors." His influence was greatly felt in the marked improvement of health of children throughout the South.

Dr. Royster was honored by membership in many distinguished fraternities and societies such as Society of the Cincinnati, Phi Beta Kappa, Alpha Omega Alpha, Sigma Chi, Sigma Xi, Raven Society, American Pediatric Society. He was a member of the American Medical Association, the Southern Medical Society, and the American Academy of Pediatrics. He was a member of the State Board of Health for over 25 years and was a member of the Committee on Growth and Development of the White House Conference.

Because of failing health he retired as professor and chairman of the Department of Pediatrics of the University of Virginia Department of Medicine in 1942. His interest in children and in his many friends in the pediatric world never ceased until his death.

Even with all the honors given him during his lifetime, he wished to be remembered with only the simple epitaph, "He Loved Children."



LAWRENCE THOMAS ROYSTER, M.D.
1874-1953

Abstracts from Current Literature

Metabolism; Infant Feeding; Milk and Other Foods

LESIONS OF GALACTOSE DIABETES: PATHOLOGIC OBSERVATIONS. LEO S. BELL, WILLIAM C. BLAIR, STUART LINDSAY, and STANDISH J. WATSON, Arch. Path. **49**:393 (March) 1950.

Galactose diabetes (galactosemia) is a rare familial metabolic anomaly occurring in infancy, which is characterized by the inability of the tissues to metabolize galactose normally. The essential clinical features of the disease are icterus, hepatomegaly, and galactosuria appearing several days after birth. Death may occur early, or the child may survive afflicted by severe malnutrition, mental retardation, or lamellar cataracts. If recognized early, these pathological changes may be reversed by eliminating milk, the source of galactose, from the infant's diet. The present concept of the hepatic alteration is one of abnormal or excessive storage of a carbohydrate in the parenchymal cells—i. e., this disease is a variant of von Gierke's disease. However, the authors did not find an excess of carbohydrate in the livers of two patients reported on. They do present, however, the findings on two siblings, with autopsy in one case and liver biopsy in the other. Excessive fatty infiltration of the liver cells and secondary degenerative changes consisting of focal necrosis and leucocytic infiltration were found. While no active fibroblastic proliferation was observed, the pathologic state was regarded as early cirrhosis.

HAW CHAN, San Francisco.

EFFECT OF PEPTONE AND AMINO ACID INGESTION UPON CONCENTRATIONS OF TISSUE AMINO ACIDS. A. LEONARD SHEFFNER and OLAF BERGEIM, J. Nutrition **48**:139 (Oct. 10) 1952.

The response of the individual free amino acid levels in muscle to the ingestion of peptone corresponded to the quantity of the respective amino acids ingested. In the liver the changes were for the most part small. The prolonged high level of lysine probably reflects the slower rate at which lysine is metabolized in the liver; the decreased arginine values indicate the increased arginase activity which occurs postabsorptively and which is associated with urea formation. In the kidney, the free amino acid levels, other than for leucine, rose in proportion to the quantities of each amino acid administered; leucine increased more than the others in proportion to the amounts ingested. The relatively high levels of leucine in all the tissues after the ingestion of food indicated that this amino acid is not utilized as rapidly, and it is suggested that it is not destroyed as rapidly, as the other amino acids. Supplementation of normal diets in rats with large quantities of racemic methionine resulted in increased concentrations of methionine in plasma and muscle but in lower levels in kidney and liver tissue. Arginine and phenylalanine levels also decreased in the kidney. On a diet containing high concentrations of racemic phenylalanine no significant changes occurred in muscle and liver tissue and in plasma; the levels of arginine and phenylalanine rose in the kidneys of fasted rats; kidney methionine concentrations did not change appreciably.

FREDEEN, Kansas City, Mo.

EFFECT OF FAT LEVEL OF THE DIET ON GENERAL NUTRITION. AMBER L. S. CHENG, GEORGE D. KRYDER, LOIS BERQUIST, and HARRY J. DEUEL JR., J. Nutrition **48**:161 (Oct. 10) 1952.

Evidence presented by Cheng and co-workers indicates that the protective action of fat is direct. In spite of the beneficial results produced by fat in lowering the mortality rate of rats following exposure to x-radiation, no concomitant improvements were noted in such indices of x-radiation injury as hemoglobin level or leucocyte count. The protective effect of fat was approximately as satisfactory when cotton seed oil was given at a 2% level as when it comprised 15 or 30% of the diet. The beneficial action of fat is therefore believed to be related to its content of essential fatty acids.

FREDEEN, Kansas City, Mo.

EFFECT OF DIETARY FAT AND CALORIC RESTRICTION ON PROTEIN UTILIZATION. HAROLD L. ROSENTHAL, J. Nutrition **48**:243 (Oct. 10) 1952.

Rosenthal's experiments demonstrate that the incorporation of large amounts of fat in the diet does not alter the utilization of dietary protein when the caloric intake is at an optimal level. However, nitrogen utilization may be reduced when large amounts of fat are fed in conjunction with diets restricted in calories and protein. The average dog can digest large amounts of protein and fat, but digestibility of fat decreases with depletion of body protein. The data also indicate the need for careful evaluation of nitrogen balance studies, so that the variables of physiological state and composition of the diet are comparable.

FREDEEN, Kansas City, Mo.

BASAL METABOLISM OF THE ESKIMO. KAARE RODAHL, J. Nutrition **48**:359 (Nov. 10) 1952.

From these studies it is concluded that there are no racial differences between the Eskimos and white persons in basal heat production.

FREDEEN, Kansas City, Mo.

EVALUATION OF BIOLOGICAL VALUES OF PROTEINS IN FISH MEALS BY THE NITROGEN RETENTION METHOD. BARNETT SURE and LESLIE EASTERLING, J. Nutrition **48**:401 (Nov. 10) 1952.

A study was made of the biological values of various fish meals by the nitrogen-retention method. All the fish meals were found to have high biological values. The lower net protein utilization of crab meal and anchovies is due to their low true digestibilities.

FREDEEN, Kansas City, Mo.

METHIONINE AND SELENIUM TOXICITY. H. L. KLUG, R. D. HARSHFIELD, R. M. PENGRA, and A. L. MOXON, J. Nutrition **48**:409 (Dec. 10) 1952.

The data of this experiment show that methionine does not prevent the toxic action of selenium compounds occurring naturally in feeds when fed to rats.

FREDEEN, Kansas City, Mo.

UTILIZATION OF CALCIUM FROM LACTATE, GLUCONATE, SULFATE AND CARBONATE SALTS BY YOUNG COLLEGE WOMEN. MARY BROWN PATTON and T. S. SUTTON, J. Nutrition **48**:443 (Dec. 10) 1952.

A study was made of the utilization of calcium by nine college women from four salts (gluconate, lactate, carbonate, and sulfate) given in amounts equivalent to 400 mg. of calcium daily. The basal diet contained an average of 347 mg. of calcium daily, and calculation of other nutrients showed that the diet was adequate. No significant differences in the utilization of calcium from these salts were found, the calcium from the less soluble salts being utilized as well as that from the more soluble ones. The data show that, regardless of the nature of the salt taken as a supplement, if it happened to be the first salt used after the preliminary adjustment period when the intake was 300 mg., its retention was greater than that for the same or any other salt at a later period. The average percentage utilization of all salts for all subjects was approximately 18%, a value within the range of those reported in the literature for utilization of calcium from food sources. An implication from these data might be that human beings do not efficiently utilize calcium from salts for periods of more than a week or two.

FREDEEN, Kansas City, Mo.

STUDIES ON THE METABOLISM AND DISPOSAL OF AMINO ACID MIXTURES GIVEN INTRAVENOUSLY. WILLIAM M. MULHOLLAND, EDWARD M. BRIDGE, and HELEN W. FOX, Pediatrics **10**:381 (Oct.) 1952.

The effects of continuous eight-hour infusions of casein hydrolysate have been studied in normal fasting rabbits. At a rate of 1.0 gm. of hydrolysate/kg./hour, approximately 5% of the

infused material is lost directly into the urine as amino nitrogen. Another 1 to 2% remains in the blood stream during the infusions but is quickly dissipated when the injection is discontinued.

Deamination, as indicated by the accumulation and excretion of urea increases steadily and proceeds at a rapid rate for approximately four hours after the infusion is discontinued. In all, 60 to 70% of the infused material may appear in the urine as urea, and another 10 to 20% in other forms. A relatively small amount is available for tissue use beyond four hours after the end of the administration.

Although retention of nitrogenous metabolites occurs during infusions at this rate and persists for several hours afterwards, renal function is not impaired.

The respiratory quotient during continuous eight-hour infusions was found to fall to the level of 0.72 to 0.74. The significance of this is uncertain.

It is suggested that relatively small amounts of complete amino acid mixtures administered continuously might supply the tissues more efficiently than much larger amounts given intermittently.

FROM THE AUTHORS' SUMMARY.

EVALUATION OF MEAT IN THE INFANT DIET. HOWARD M. JACOBS and GEORGE S. GEORGE, Pediatrics **10**:463 (Oct.) 1952.

A commercially prepared lean meat was fed to young infants as a suplement to a diet already adequate in all food factors. In those infants first fed meat under 2 months of age, there was improvement in physical growth as determined by weight and height measurements. The same group demonstrated an improvement in hemoglobin levels and elimination of the physiologic drop in total protein levels of the serum, with a prompt sustained rise in values, the greater part of which was composed of the globulin fraction. In those infants first fed meat after 2 months of age, there was a slight improvement in average weight gain, but no significant difference was noted in other body measurements, total protein, albumin or globulin fractions, or hemoglobin levels.

Illness rates for the two years of the study demonstrated a 40% lower morbidity rate in the meat-fed group as compared with the control group. In striving for the optimum in infant nutrition protein requirements should be evaluated both quantitatively and qualitatively.

FROM THE AUTHORS' SUMMARY.

ELECTRON-MICROSCOPIC EXAMINATION OF HUMAN MILK PARTICULARLY FROM WOMEN HAVING A FAMILY RECORD OF BREAST CANCER. LUDWIK GROSS, ALBERT E. GESSLER, and KENNETH S. MCCARTY, Proc. Soc. Exper. Biol. & Med. **75**:270 (Oct.) 1950.

Small spherical particles, 20 to 200 μ, have been visualized with the aid of an electron microscope in samples of milk obtained from nursing mice known to carry the mammary carcinoma. This observation prompted the authors to study human subjects. They obtained samples of milk from young healthy women who had delivered three to seven days previously and were nursing at the time. Two groups of women were selected. From the first, women whose sisters, mothers, or grandmothers had breast cancers, 10 milk samples were collected. From the second women with a family history negative for malignant tumors for two preceding generations 32 samples were obtained. Altogether, a total of 396 electron micrographs were taken from the samples examined. Particles were found in all 10 samples from mothers with a family history of breast cancer. These particles were of high density and appeared to have a regular round shape and smooth surface, and varied in diameter from 2 to 20 μ. In 5 of the 10 samples the particles were rather numerous, and appeared similar to those found in mouse milk. Spherical particles were found in 11 of the 32 samples from the second (control) group; some of them were in pairs or clusters, but in 5 samples they were present in large numbers. In the remaining 21 control samples of this group, there were only very few, mostly isolated, spherical particles, although in size and form they were not different from those previously desscribed. The other four samples appeared to be free from spherical particles but contained some identifying debris. The authors feel that no definite conclusions can be reached at this time as to the nature of the spherical particles.

HANSEN, Galveston, Texas.

PROTEIN REQUIREMENTS OF INFANTS. P. POYNER-WALL and E. FINCH, Arch. Dis. Childhood **25**:133 (June) 1950.

Total protein, albumin, and globulin concentrations have been estimated in the serum of a series of normal full-term infants whose ages ranged from 36 hours to 1 year. The levels were estimated by micro-Kjeldahl digestion followed by direct nesslerization; this method tends to give lower results than those obtained by micro-Kjeldahl digestion followed by titration.

A very wide scatter for all three concentrations was found throughout this period of infancy. The average total serum protein levels showed a slight initial fall during the first few weeks of life, followed by a rise to the original level by 3 months of age, and a further slight rise as the age approached 1 year. These changes were due to variations in both the albumin and the globulin fractions.

KELLY, Milwaukee.

ESTIMATION OF SERUM PROTEIN CONCENTRATIONS. I. BROADBENT and E. FINCH, Arch. Dis. Childhood **25**:134 (June) 1950.

The average of a series of serum protein concentrations estimated by the nesslerization method (Hickmann, 1948) was slightly lower (0.22 gm. of protein per 100 ml.) than the average of the same series determined by a titration method. Since the error of the nesslerization method is not a consistent one, no correction can be applied to individual results which have been obtained by this method. If, however, the serum protein concentration in a sufficiently large number of cases has been estimated, the effect of individual errors on the average of the results is reduced and it is possible to assess the findings. Nevertheless, when small variations in serial specimens are to be estimated, the titration method is preferable, in spite of the fact that it requires a little more serum.

KELLY, Milwaukee.

SERUM INDICAN AND SERUM XANTHOPROTEIN VALUES IN CHILDREN. HERIBERT BERGER, Ann. pædiat. **175**:49 (July-Aug.) 1950.

The serum indican and the serum xanthoprotein value were ascertained in 37 patients of the children's hospital, Berne University, ranging in age from 1 month to 16 years. The normal value for serum indican was found to be 0.03 to 0.09 mg. per 100 cc.; for the xanthoprotein it was 25 to 30 mg. No parallelism between these two values could be discovered. A regular, but not very important, rise of the serum indican value was found in patients with active tuberculosis and in a few patients with poliomyelitis. A slight rise was also observed in a patient with celiac disease, a marked one in a dystrophic patient with a cerebral disturbance, and a very high value, in a patient with secondary nephrosclerosis. In patients with nephrosis the values are normal. Since patients with raised xanthoprotein values were rare, the author did not feel entitled to draw any conclusions with regard to the pathological occurrences. A theoretical part in the introduction deals with the formation of indican in the organism and with the character of the xanthoprotein reaction. The method employed was colorimetric.

FROM THE AUTHOR'S SUMMARY.

ADVANCES IN DIETETIC THERAPY. E. GLANZMANN, Helvet. paediat. acta **5**:401 (Nov.) 1950.

The significance of the essential amino acids for growth and repair, for formation of enzymes and hormones, and for production of germ cells, antitoxins, and other antibodies is discussed. The great demand for proteins of premature infants, due to rapid growth, cannot be met by mothers' milk alone. The addition of amino acid mixtures in 0.5 to 1% solutions has, therefore, often proved a useful procedure. Such amino acid mixtures can also perform valuable services in cases of hypoproteinemia (protein deficiency disease), celiac disease, cystic fibrosis of the pancreas, nephrosis, blood disorders, epidemic jaundice, cirrhosis of the liver, etc. Individual amino acids have their special indications, e. g., methionine in cases of hepatic disease and glutamic acid in cases of developmental disorders of the nervous system.

The so-called vitamin T of Goetsch is probably related to as yet unspecified amino acids. The vitamin T complex was first gained from insects and later also from yeasts (Cryptococcus [Torula] utilis). In children, one could also record, in accordance with Nussbaumer, remarkable

results, with good weight increase, on administration of 10 drops of vitamin T two to three times daily for three weeks. After a three-week period the treatment must be interrupted for 7 to 14 days, since otherwise a negative phase ensues.

The success noted in the treatment of eczema with unsaturated fatty acids, particularly with lard (10, 30 or 60 gm. daily), is of special interest. Fresh lard contains 5 to 11% unsaturated fatty acids; it has a very favorable effect on eczema, though not in all cases. A secondary eutrophic effect is also noteworthy, although it is not as pronounced as in the essential amino acids, especially in combination with vitamin T.

Finally, the use of waste substances from apples, carrots, and carob flour in the treatment of infantile diarrhea is discussed. The good response is due to the action of a binding material, such as the pectins and, in carob, especially lignins, which bind together the small particles to form a homogenous stool. Initial difficulties can be overcome by boiling "arobon" (carob flour) for 10 minutes with final addition of 1% skimmed or whole "eledon" powder. The diatetic treatment of dyspepsias and toxicoses is briefly described.

FROM THE AUTHOR'S SUMMARY.

A CASE OF CYSTINOSIS. C. MONOD, Helvet. paediat. acta **6**:534 (Dec.) 1951.

A case of familial cystinosis, presenting the classic clinical features, is described. The disease was diagnosed clinically by the finding of crystals of cystine in the bone marrow, in the conjunctiva, and in the cornea.

FROM THE AUTHOR'S SUMMARY.

METABOLIC ASPECTS OF PRIMARY ERYTHROBLASTIC ANEMIAS OF INFANT: BEHAVIOR OF THE TOTAL FATTY ACIDS, SATURATED AND UNSATURATED, OF THE BLOOD. G. CADEDDU, Ann. ital. pediat. **3**:261, 1950.

The author, in a study of the fatty acids in the blood of children with subchronic erythroblastosis and Cooley's disease, has established an increase of total fatty acids with a higher percentage of the unsaturated fraction and ensuing increase of the unsaturation index. He reports the results of an experiment to stimulate the erythropoiesis with folic acid and the results of an attempt to balance the fatty acids with paraaminobenzoic acid.

The author concludes from his experiments that it is impossible to establish a relation between the nature and the intensity of the erythroblastic phenomenon and the modifications of the fatty acids in the blood. He believes instead that these modifications, as a generic phenomenon, can be referred to the alterations of the metabolic process provoked by severe anemia.

FROM THE AUTHOR'S SUMMARY.

MILK CURDS. M. LUST, Lattante **23**:385 (July) 1952.

The various means for obtaining soft curds in milk to be used in infant feeding are discussed, boiling, dilution with water, addition of calcium lactate or calcium gluconate or starch, and homogenization.

HIGGINS, Boston.

THE ACTION OF BILE ACIDS AND SALTS AND OF LIPOCAIC (P) ON THE CLINICAL AND METABOLIC PICTURE OF GLYCOGEN STORAGE (VON GIERKE'S DISEASES). R. BULGARELLI, Minerva pediat. **2**:122 (March) 1950.

A boy, a dwarf with von Gierke's disease, was given daily, over a period of 9 months, 0.75 gm. of dehydrocholic acid by mouth, and 10 cc. 20% solution of sodium dehydrocholate by injection. As a result of this treatment, the liver became smaller, the blood chemistry tended to approach the normal, urobilin and acetone in the urine diminished, and glycogen utilization seemed to improve. Two and a half months' treatment with lipocaic (equivalent of 18 gm. of fresh pancreas and 129 mg. of choline hydrochloride daily) led to similar improvement clinically, except that the glycogen utilization was diminished.

HIGGINS, Boston.

THE ABSORPTION AND UTILIZATION OF FAT IN INFANTS FED A MILK WITH HIGH PERCENTAGE OF TRIOLEIN. G. CAFFARENA, Minerva pediat. **2**:134 (March) 1950.

Fat retention was found to be greater in babies fed a proprietary milk preparation which contained a high percentage of triolein (Pantolac) than in those fed a chemically similar formula which contained fat derived from cream. Clinically, in a series of 20 babies, the milk preparation was found to be a satisfactory food.

HIGGINS, Boston.

A CASE OF ADOLESCENT OBESITY. C. SÁINZ DE LOS TERRERAS and M. TALOSO LATOUR, Acta pediat. españ. **117**: (Sept.) 1952.

The authors report on the case of an 8-year-old boy with polydypsia, polyuria, and polyphagia for a period of two months. This complex was also associated with febrile episodes and a gain of 6 kg. in weight. The family history included acromegaly in the father and a grandfather, syphilis in a maternal grandmother, and hermaphroditism in a paternal uncle. With such a history, the differential diagnosis between various forms of obesity was quite important. Conditions such as Cushing, Appert-Gellert, Fröhlich's, and Lawrence-Moon-Biedl syndrome might be responsible for the obesity. According to the table in the Mitchell-Nelson textbook, this is a typical case of adolescent obesity. Complete physical examination revealed nothing unusual except the obesity and an undescended testis; the penis was normal, however.

Laboratory findings indicated that the family's complaint of excessive urination and drinking was relative rather than actual. The basal metabolic rate was —7.5%. Blood chemistry and glucose tolerance tests were normal. Blood counts, and serological examinations, and x-rays including the sella turcica were negative. The eyegrounds were also normal.

Thyroxin was used with no results. On ward observation for 16 days no febrile episodes developed and the patient's diet, when the protein and amino acid content was increased, tended to control his gain in weight.

ALLEN, San Francisco.

STUDIES IN UNDERNOURISHED INFANTS: HEPATIC FUNCTION. F. GÓMEZ, R. RAMOS, GALVAN B. BIENVENU, and J. MUNOZ CRAVIOTO, Bol. med. hosp. inf., Mexico **7**:485 (Aug.) 1950.

Sulfobromophthalein (bromsulphalein) sodium and direct and indirect van den Bergh tests were performed on a group of malnourished children, without any abnormal results.

Cephalin-cholesterol flocculation and thymol turbidity tests were performed on 50 healthy children. The same tests were performed on 58 children with simple malnutrition and 48 children with pellagra, who were studied separately according to whether or not infection was present.

Results of thymol and cephalin-cholesterol tests in preschool children studied were as follows:

1. In children with simple malnutrition, slight or advanced, the results were normal.

2. Normal results were also obtained in children with pellagra without infectious complications.

3. The abnormal thymol results found in malnourished or pellagrous children may be attributed to infection or to hepatic regeneration processes.

4. The abnormal results of the cephalin-cholesterol test in malnourished or pellagrous children may be ascribed exclusively to infection.

FROM THE AUTHORS' SUMMARY.

STUDIES ON UNDERNOURISHED INFANTS: PROTEIN FRACTIONS. F. GÓMEZ, R. RAMOS, GALVAN J. MUNOZ CRAVIOTO, and B. BIENVENU, Bol. med. hosp. inf., Mexico **7**:504 (Aug.) 1950.

The authors report on the results obtained in determining the blood and plasma volumes in healthy preschool children, given the weight, height, or their body surface area; standard calculation errors are reported. Stress is laid on the fact that the most precise relation to the plasma volume is that in which the surface area is used in the calculations, since weight and height suffer variations with age. Charts are presented to illustrate these concepts.

FROM THE AUTHORS' SUMMARY.

STUDIES ON UNDERNOURISHED INFANTS: BLOOD VOLUME AND BLOOD PLASMA. F. GÓMEZ, R. RAMOS GALVAN, J. MUNOZ CRAVIOTO, and B. BIENVENU, Bol. med. hosp. inf., Mexico **7**:514 (Aug.) 1950.

The authors report the results on the study of blood and plasma volumes in 70 children with malnutrition. A comparison is made with the figures reported for healthy children, finding that malnourished children show on increase in both volumes (blood and plasma) expressed in cubic centimeters per kilogram of body weight; that is, the severer the malnutrition the greater the blood volume per kilogram of body weight.

Owing to the histologic findings in the liver of malnourished children and to Himsworth's works, the authors believe that one of the causes that produces an increase in the plasma volume may be ascribed to the vasodepressor factor, which originates in the diseased hepatic cells.

FROM THE AUTHORS' SUMMARY.

UNIDIMENSIONAL PAPER PARTITION CHROMATOGRAPHY. JOSEF ŠVEJCAR and JAROSLAV HNATEK, Pediat. listy **5**:250, 1950.

A series of twelve infants and toddlers with rickets, six of whom were vitamin-D resistant, were examined. In two of the children, 2½ and 3 years old respectively, with definite signs of rickets (thorax deformities) a constant urinary excretion of amino acids which normally are not present in the urine was found by means of the unidimensional paper partition chromatography (mostly bicarbonic hydroxyamino and monoamino carbonic acids with a high molecular weight). Both children are considered to be suffering from a beginning aminic diabetes. The parents of both children had been suffering from a severe form of late rickets, which brought about lasting deformities. The two children have now been followed up for longer than a year; all through this time the amino acid elimination has not ceased. Their general health and development has been satisfactory under treatment with massive doses of vitamin B and D preparations.

FROM THE AUTHORS' SUMMARY.

VARIATIONS OF THE VITAMIN H-LEVEL IN MOTHERS' MILK DURING A PERIOD OF 12 MONTHS (SEPTEMBER, 1948-AUGUST, 1949). J. HOMOLKA and J. RÍMAN, Pediat. listy **6**:326 (Sept.) 1950.

A level of 1.3 to 1.5 γ of biotin in mother's milk is regarded as the physiological level.

The number of babies with desquamative erythroderma (Leiner disease) increases during the months of lowered level of biotin in the milk of nursing mothers.

Crises in babies caused by the insufficiency of biotin can be prevented by suitably adjusting the food given to nursing mothers.

FROM THE AUTHORS' SUMMARY.

STAUB EFFECT IN CHILDREN: STUDIES OF BLOOD SUGAR REGULATIONS BY MEANS OF DOUBLE AND TRIPLE GLUCOSE TOLERANCE TESTS. OLLI SOMERSALO, Acta pædiat. Supp. 78, p. 1, 1950.

A series of 27 intravenous double and triple glucose tolerance tests were performed on children 1 to 12 years old. The interval between the injections varied from 40 to 200 minutes and the dose varied from 0.25 to 2 gm. per kilogram of body weight. The curves were compared by using the criterion of their length, i. e., the falling time to 0.1%. Not a single instance revealed an unmistakably more rapid fall of the second curve to 0.1%—no Staub effect appeared—provided that the second tolerance test was performed after the return to normal of the first curve. In experiments in which the interval between injections exceeded 60 minutes, a slightly negative Staub effect was obtained as a rule—the second curve descended more slowly than the first.

Eight similar experiments were performed on adults. They showed the Staub effect as it is reported in the literature, with the exception of one case, in which the first curve fell more rapidly than normal (test person 31). Both those experiments in which the interval between injections was very long also revealed a negative Staub effect as obtained in similar tests performed on children.

In 22 peroral double tolerance tests the Staub effect appeared as a rule, but there were 5 clearly inverted reactions. This result was obtained particularly in those tests in which the first peroral curve was very low.

However, the peroral double tolerance test gives an unreliable picture of the blood sugar regulation, since both these tests were affected by several accidental factors, such as the evacuation rate of the stomach and the rate of absorption. If the effect of the peroral tolerance test on the blood sugar regulation is to be studied, the second peroral test is therefore an unreliable indicator. If, instead of this second peroral test, an intravenous dose is administered and this intravenous curve is compared to a similar, earlier one, the change in the blood sugar regulation induced by the peroral curve will in all probability be obtained with greater exactitude. Since the second intravenous test was not greatly affected by the first, this standard curve was obtained in several cases by administering the intravenous dose immediately before the peroral one. Of these intravenous-peroral-intravenous tests, 30 in all were performed on children aged 1 to 13 years. It was noted as a result that the second intravenous tolerance curve was, as a rule, shorter than the first and that this shortening was pronounced particularly in those tests in which the peroral dose produced a very slight elevation of the blood sugar. By determining the catalyzation—shortening of the intravenous curve—both as a percentage and in minutes, it was observed that a negative correlation exists between the peroral maximum height and the catalyzation and, similarly, between the area of the peroral curve and catalyzation.

It is concluded that the intravenous glucose tolerance test did not accelerate the blood sugar regulation in children; instead, this effect was brought about by the peroral dose, although it produced a much slighter elevation of the blood sugar or none at all. This leads to the conclusion that the mechanism of the Staub effect is influenced by some agent other than those already assumed, such as increased insulin secretion, activation of insulin in the liver, or a reduced glycotropic secretion of the anterior pituitary. These could all be regarded as highly pronounced under the influence of strong hyperglycemia during intravenous tolerance tests and can hardly be assumed to occur at all under the influence of those peroral tolerance tests which do not elevate the blood sugar in the extraportal circulation.

This factor probably exercises its effect during the absorption of glucose or its passage through the portal circulation; therefore it could be either the increase of the minute volume of the liver or the presence of some substance reducing blood sugar, liberated in the intestine during the process of absorption. The Staub effect manifested in children is, in all probability, mainly produced by this factor. The negative correlation between the maximum height of the peroral curve and catalyzation is easy to interpret; namely, that the stronger this factor, the slighter the rise of the peroral curve and the greater its shortening effect exercised on the following intravenous curve.

FROM THE AUTHOR'S SUMMARY.

Vitamins; Avitaminoses

VITAMIN A UTILIZATION STUDIES: IV. RELATIVE UTILIZATION OF VITAMIN A-ALCOHOL, VITAMIN A-ACETATE AND VITAMIN A NATURAL ESTERS AS AFFECTED BY VARIATIONS IN DOSAGE LEVEL, QUANTITY AND CHARACTER OF DILUENT, AND QUANTITY OF DIETARY FAT. ERLING F. WEEK and FRANK J. SEVIGNE, J. Nutrition **42**:525 (Dec. 11) 1950.

Week and Sevigne investigated the effects of variations in the type and quantity of diluent, the fat content of the basal diet, and the level of vitamin A intake on the relative biological utilization of vitamin A-alcohol, acetate, and natural esters by the rat. Liver storage measurements were used as the criterion of utilization. Liquid petrolatum and ethyl laurate were shown to contain factors which inhibit hydrolysis of vitamin A ester in vivo.

FREDEEN, Kansas City, Mo.

THIAMINE METABOLISM OF WOMEN ON CONTROLLED DIETS: I. DAILY URINARY THIAMINE EXCRETION AND ITS RELATION TO CREATININE EXCRETION. HELLIN A. LOUHI, HSI-HSUAN YÜ, BETTY E. HAWTHORNE, and CLARA A. STORVICK, J. Nutrition **48**:297 (Nov. 10) 1952.

When eight normal women were maintained on an intake of 500 γ of thiamine per 1,000 Cal., the average daily urinary excretions of thiamine ranged from 100 to 276 γ. With the thiamine

reduced to 300 γ of thiamine per 1,000 Cal., the average daily urinary excretions ranged from 34 to 109 γ. When an excretion of 100 γ of thiamine per 24 hours, an excretion of 13% of the daily thiamine intake, and an excretion of 150 γ of thiamine per gram of creatinine were used, as indications of good nutrition with respect to thiamine, an intake of 500 γ of thiamine per 1,000 Cal. was judged to be adequate for six of the eight patients and borderline for the other two. An intake of 300 γ of thiamine per 1,000 Cal. was inadequate for six of the subjects and borderline for the other two. The response of 4 subjects to a 5 mg. oral test dose of thiamine hydrochloride given on the last day of the period of lowered thiamine intake indicated that the tissues of all the subjects were low in thiamine.

FREDEEN, Kansas City, Mo.

THIAMINE METABOLISM OF WOMEN ON CONTROLLED DIETS: II. DAILY BLOOD THIAMINE VALUES. RACHEL B. DUBÉ, ELIZABETH COX JOHNSON, HSI-HSUAN YÜ, and CLARA A. STORVICK, J. Nutrition **48**:307 (Nov. 10) 1952.

With an intake of about 500 γ of thiamine hydrochloride per 1,000 Cal., the average fasting blood thiamine ranged from 3.3 to 5.4 γ per 100 ml. of whole blood or 7.0 to 11.2 γ per 100 ml. of packed cells. When the intake was lowered to 300 γ of thiamine hydrochloride per 1,000 Cal., the average fasting blood thiamine ranged from 2.8 to 4.6 γ per 100 ml. of whole blood or 6.3 to 10.0 γ per 100 ml. of packed cells.

FREDEEN, Kansas City, Mo.

INFLUENCE OF VITAMIN B_{12} AND ANTIBIOTICS ON PROTEIN AND ENERGY UTILIZATION IN A LOW PROTEIN DIET. LEON K. KNOEBEL and ALEX BLACK, J. Nutrition **48**:477 (Dec. 10) 1952.

In this work Knoebel and Black show that food is better utilized after absorption from the intestinal tract when vitamin B_{12} and antibiotics are present than when these supplements are absent.

FREDEEN, Kansas City, Mo.

MELANOKERATOSIS SCORBUTICA. W. EHRENGUT, Ann. paediat. **175**:413 (Dec.) 1950.

Ehrengut investigated two cases of infantile scurvy showing the rather overlooked hyperpigmentation which sometimes occurs with this disease; in one case they were combined with keratosis. After explaining the relations of the adrenals, vitamin C, and the pigment metabolism in Addison's and Graves's disease, the pigment formation and the role of ascorbic acid are discussed. The hypothesis is made that melanosis in scurvy is due to a reduced content of the skin in vitamin C and sulfhydryl groups, these substances being probably united in the redox-system. A correlative disturbance in the level of vitamins A and C is considered to form an etiological factor for scorbutic keratosis. Because of the general dystrophy and the lack of vitamin C, damage to the endocrine glands, especially the adrenals, has to be assumed. The similarity to the melanosis of Riehl is pointed out, and the raised blood copper level in that disease is stressed; the raised level is explained as a sign of increased thyroid function.

FROM THE AUTHOR'S SUMMARY.

VITAMIN B IN PEDIATRICS. W. SWOBODA, Wien. klin. Wchnschr. **64**:276 (April 11) 1952.

Patients with chorea minor have been treated the last two years with pyridoxine, with good results in the majority. In cases in which definite rheumatic, particularly cardiac, symptoms existed, aminopyrine was given in combination. A case is cited very briefly, in which pyridoxine was given in the presence of a mitral lesion. The carditis was exacerbated and the patient died within 48 hours. The impression was gained that myotonia congenita responded to this treatment better than Erb's muscle dystrophy. Acetonemic vomiting in early childhood ceased promptly on administration of pyridoxine.

AMBERG, Rochester, Minn.

INJURIES DUE TO OVERDOSAGE OF VITAMIN D. O. RUZICZKA, Wien. Klin. Wchnschr. **64**:964 (Dec. 12) 1952.

A vitamin D_3 preparation containing 6.25 mg. (250,000 I.U.) per cubic centimeter was given to children in teaspoon doses one to three times a day or even in tablespoon doses (20 to 95 mg.

daily orally) in the belief that cod liver oil was being administered. The preparation was given for various lengths of time. Because of the excessive dose given, the smaller children were taken ill after three to nine days, the older ones after two to three weeks. The smallest total amount before illness amounted to 100 mg. (4,000,000 I.U.). Many children received 200 to 450 mg. (8,000,000 to 18,000,000 I.U.) or even more. Of the 23 children 3 died, 14 were severely, and 6 slightly ill. The ages of the children at the onset of treatment were 6 months to 12 years. The less seriously ill children had loss of appetite, vomiting, and stomach disorders and were irritable but did not require bed rest. With cessation of medication, the symptoms disappeared in a day or a few days. In the severely ill, these symptoms were more pronounced with addition of abdominal spasms. The loss of fluid by vomiting became prominent, and temperatures up to 104 F. were registered. The children were tired, anxious, and apathetic. Some were somnolent, others had sleeping difficulties. Several complained of pains in extremities or the whole body. Of the four who were taken with tonic-clonic convulsions, three died. The severe manifestations disappeared slowly. Results of the examination of blood, serum, and urine, of x-ray examination, and of histological sections are to be given elsewhere.

AMBERG, Rochester, Minn.

VITAMIN D REQUIREMENTS OF OLDER CHILDREN WITH REFERENCE TO CONDITIONS IN ADULTS. FRITZ KÜSTER, Ztschr. Kinderh. **68**:437, 1950.

From a review of the literature the author concludes that vitamin-D deficiency exists in older children, although customarily prophylactic doses of vitamin D are given only to infants and small children. In 30 children between the ages of 9 and 11 years he found a rise in serum inorganic phosphorus of about 0.5 mg. per 100 cc., following the administration of 15 mg. of a vitamin D preparation ("vigantol"). Repeated tests showed that three and one-half months later the increased phosphorus levels were maintained. The change of 0.5% proved statistically significant. From this, the author concludes that there is not only a need for vitamin D prophylaxis throughout the growth period but also in adulthood. Vitamin D-enriched milk seems the best form of administration.

GLASER, Jerusalem.

Hygiene; Growth and Nutrition; Public Health

TREATMENT OF GROWTH FAILURE IN ALEUT SCHOOL CHILDREN. EDWIN WILDE, J. Pediat. **40**:565 (May) 1952.

A study of nine Aleut school children indicates that in some children growth failure is a manifestation of functional deficiency of vitamin B_{12}, which may be corrected by oral administration of vitamin B_{12}.

MACDONALD, Pittsburgh.

INFANT MORTALITY AND THE SOCIAL SERVICES. STANLEY GRAHAM, Canad. M. A. J. **67**:323 (Oct.) 1952.

The author reviews figures on infant mortality and correlates them with social status of the parents. He points out the definite rise in mortality as the social status becomes lower. It is suggested that the infant mortality rate can now be strikingly reduced by raising the living conditions of all to the highest possible level.

MCGUIGAN, Evanston, Ill.

BIRTH AND DEATH RATES IN INFANTS UNDER 1 YEAR OF AGE IN THE PROVINCE OF PADUA DURING THE PAST 14 YEARS, WITH PARTICULAR ATTENTION TO TWINS AND TRIPLETS. D. AGOSTO, Lattante **22**:14 (Jan.) 1951.

The death rate per 1,000 births in infants under 1 year of age in the province of Padua averaged 78 in the prewar years, 76 in the war years, and 58 in the postwar years. The number of births in the province was 10% lower in the postwar years than in the prewar years. Congenital debility and malformations are now the commonest cause of infant deaths, followed in order by nutritional disorders, respiratory infections, and contagious diseases. The percentage of twin parturitions in 1949 was 12.5 and of triplet parturitions 0.6. One-third of the twins and over half of the triplets died in the first year of life. Congenital debility and malformations caused 72% of the deaths in twins and 81% of the deaths in triplets.

HIGGINS, Boston.

STATISTICAL SOMATOMETRIC STUDY OF 1,000 CHILDREN BETWEEN 0 AND 14 YEARS, BY MEANS OF THE WIDTH-HEIGHT INDEX. CARLOS A. BAUZA and SOLOVEY DE MILECHNIN G., Arch. pediat. Uruguay **21**:997 (Dec.) 1950.

The authors describe their experience with the width-height index, postulated by Lucas and Pryor for assessing body build. The somatotype of the male shows an increasing "linearity" until 14 years of age. The somatotype of the female shows an increasing "stockiness" until 14 years of age.

The male is stockier than the female from birth until 9 years; thereafter the female becomes stockier than the male. Until the age of 9 or 10 years the male shows a greater bicrestal diameter than the female; the mean value of this difference is 4.6 mm. for the school children and 2.0 mm. for the hospital children. Around 10 years, girls surpass boys in bicrestal diameter, the mean value of this difference being 18.6 mm. for school children up to the age of 13.5 years. The anthropometric measurements of school children then differ from those taken in hospital children. School boys (mean 5.0 cm.) and school girls (mean 3.9 cm.) are taller than hospital children of the same age. School boys (mean 10.3 mm.) and school girls (mean 15.4 mm.) have a larger bicrestal diameter than hospital children of the same age. School children are constantly stockier than hospital children.

The mean stature of Uruguayan school children between 6½ and 13½ years of age shows an increase when compared with a standard height-weight-age table made 20 years ago; the mean increase in stature is 4.7 cm. for males and 4.5 cm. for females.

FROM THE AUTHORS' SUMMARY.

Prematurity and Congenital Deformities

RETROLENTAL FIBROPLASIA. MARY LOUISE NEWMAN, Illinois M. J. **100**:245 (Oct.) 1951.

In this review Newman reports that retrolental fibroplasia was first described 10 years ago and is increasing at an alarming rate. This increase parallels the increased salvage of very small premature infants. In a personal investigation she learned that this general trend is equally true in Illinois. At the present rate of increase, authorities estimate that retrolental fibroplasia will soon be one of the chief causes of blindness in schools for the visually handicapped. There is no known established therapy. The main problem is one of prevention.

BARBOUR, Peoria, Ill.

FUNCTIONAL INTESTINAL OBSTRUCTION IN THE PREMATURE NEWBORN INFANT. FRANK J. RACK and WALTER L. CROUCH, J. Pediat. **40**:579 (May) 1952.

The authors report on a premature newborn infant with intestinal obstruction not associated with a recognized congenital anomaly and not due to meconium ileus. This infant passed meconium and later normal stools for one week after birth. Signs of obstruction appeared on the ninth day. At operation the entire colon, from cecum to rectum, was found filled with a stony hard cast that resisted attempts to "milk" it along into the rectum for manual extraction. The fecal concretions were evacuated through multiple colotomies. After primary closure and a stormy convalescence, the patient did well.

MACDONALD, Pittsburgh.

REDUCTION OF MORTALITY IN THE PREMATURE NURSERY. HARRY BLOCH, HOWARD E. SCALETTAR, BERNARD REDNER, and DANIEL HIRSCHL, J. Pediat. **40**:584 (May) 1952.

In the modern premature nursery the influence of postnatal infection on the fatality rate is insignificant. A premature nursery conducted as advised by the American Academy of Pediatrics is the best method of safeguarding infants from postnatal infection.

MACDONALD, Pittsburgh.

RETROLENTAL FIBROPLASIA: CLINICAL OBSERVATIONS. W. R. HEPNER JR. and ARLINGTON C. KRAUSE, Pediatrics **10**:433 (Oct.) 1952.

Retrolental fibroplasia is a postnatally acquired disease. The basic pattern for the disease is present in the majority of premature infants born weighing less than 1,500 gm. A relationship

between the electrolyte content of the diet and fluid retention can be established in small premature infants. A relationship between large blood transfusions and an increased incidence of retrolental fibroplasia is presented. Exclusively human milk diets, fed until a weight of 1,800 gm. is achieved, do not prevent development of the disease later in infants born weighing less than 1,500 gm. Corticotropin may exert its temporary influence on retrolental fibroplasia by its diuretic effect on water and salt metabolism in the premature infant.

Two factors, formulas of high electrolyte concentration and blood transfusion, may overload the capacities for physiologic adjustment of the smaller premature infant, and lead to the disease. A direct relationship between the development of retrolental fibroplasia and blood transfusion during a period of water and electrolyte retention is reported. The practice of feeding high-electrolyte formulas, and excessively large blood transfusion for anemia, may be responsible for the remarkable variation in incidence from hospital to hospital, the variation in incidence even in the same hospital, and the increasing incidence of the disease in premature infants following the introduction of these practices.

FROM THE AUTHORS' SUMMARY.

ASSESSMENT OF PREMATURITY BY BIRTH WEIGHT, CROWN-RUMP LENGTH, AND HEAD CIRCUMFERENCE. RICHARD W. B. ELLIS, Arch. Dis. Childhood **26**:421 (Oct.) 1951.

Measurements of occipitofrontal head circumference, crown-rump length, and birth weight have been made on 119 living premature infants of 29 to 37 weeks' gestation inclusive and on 243 male and 209 female full-term infants. Crown-heel length was measured on 30 premature infants and on 238 male and 206 female full-term infants. The means and standard deviations for groups of increasing gestational age are presented, and the frequency distributions and correlations for each measurement are given in the case of full-term infants.

It is suggested that crown-rump length might usefully be included in the routine measurement of infants where facilities are available, and it is emphasized that this measurement has certain advantages over that of crown-heel length in the case of premature infants.

The criteria of prematurity are discussed. The following arbitrary measurements were found to fit the data sufficiently well to be of clinical value: head circumference less than 33 cm. (13 in.); crown-rump length less than 32 cm. (12⅝ in.) or alternatively 31.75 cm. (12½ in.) or less; birth weight 2,500 gm. (5½ lb.) or less. It is emphasized that any single arbitrary standard is likely to include a proportion of full-term infants and exclude a proportion of premature of over 36 weeks' gestation. The proportion of misfits will be reduced by using three or more measurements in combination, together with gestational age when this is known. Although it does not at present appear practicable to recommend different standards of prematurity for males and females, the proportion of misfits will be affected by sex.

KELLY, Milwaukee.

INTRAUTERINE FETAL DAMAGE FROM EPIDEMIC HEPATITIS. T. F. HELLBRUGGE, Ann. pædiat. **179**:226 (Oct.) 1952.

A short survey is given of the literature concerning the known virus embryopathies. It is followed by the description of a case from the University Policlinic in Munich. Besides physical and mental retardation there were developmental disturbances in both eyes (right: microphthalmus, congenital coloboma iridis, nervi optici et chorioideae; left: incomplete coloboma iridis), and cerebral malformations amounting to microgyria with simultaneous dilatation of a part of the internal cerebral cistern.

The termination period of these anomalies—fourth to fifth week of pregnancy—coincides in this case with the mother's jaundice. From the clinical history it can be assumed that this was due to a virus hepatitis.

FROM THE AUTHOR'S SUMMARY.

APPEARANCE OF FUNDUS OCULI IN PREMATURE INFANTS, WITH SPECIAL REFERENCE TO THE EARLY STAGES OF RETROLENTAL FIBROPLASIA. A. HUGGERT, Acta pædiat. **41**:463 (Sept.) 1952.

A regular examination of the fundi of 66 premature infants was carried out each week from birth. Among these cases there were 18 that presented a fundus picture similar to that described as being typical for early retrolental fibroplasia. These changes were reversible in all cases.

Minor changes taking the form of a yellow-white color and a slight edema in the periphery of the fundus were observed in two-thirds of the total material. If one considers the time at which these changes were first manifest in relation to birth, it would appear that the greater the birth weight the sooner changes become apparent. In view of this fact and the high incidence of these minor fundus changes, it is suggested that the changes described in this paper and in the early stages of retrolental fibroplasia are merely normal stages of development.

FROM THE AUTHOR'S SUMMARY.

Newborn

FACIAL ASYMMETRY IN THE NEWBORN INFANT: ITS RELATION TO CONGENITAL CRANIAL OSTEOPOROSIS (CRANIOTABES) AND INFANT BIRTH ORDER. ELENA BODER, J. Pediat. **40**:558 (May) 1952.

Facial asymmetry occurs more frequently in the newborn of primiparas than in those of other mothers probably because of intrauterine mechanical-postural causes. There is evidence that congenital cranial osteoporosis is a contributing factor in some cases. Postnatal head and facial asymmetries and dentofacial deformities sometimes follow. Since avitaminosis D during pregnancy may lead to congenital cranial osteoporosis, antepartum administration of vitamin D to the mother may help to prevent these deformities.

MACDONALD, Pittsburgh.

GANGRENE OF THE EXTREMITIES IN THE NEWBORN INFANT: REPORT OF TWO CASES. WILLIAM E. ASKUE and RUTH WONG, J. Pediat. **40**:588 (May) 1952.

Gangrene of the extremities in the newborn is rare. Possible causes are birth trauma, emboli from thrombotic closure of the ductus arteriosus, and thrombosis of the umbilical arteries. Early and vigorous treatment is indicated.

MACDONALD, Pittsburgh.

STOOL FREQUENCY OF NORMAL INFANTS IN THE FIRST WEEK OF LIFE. WILLIAM L. NYHAN, Pediatrics **10**:414 (Oct.) 1952.

The stool frequency of 800 normal infants during the first week of life was studied statistically. The series was composed of 400 infants fed on a flexible regimen of whom 200 were breast fed and 200 were bottle fed, and 400 infants fed on the conventional four hour schedule, of whom 200 were breast fed and 200 were bottle fed. Analyses were made with respect to number of stools and variability. The normal pattern was that of rise in both number of stools and variability up to the fifth day and a gradual fall. The peak for both number and variability occurred in the period from the third to the sixth day. The range of variation about the mean on each day was quite great, and this fact seemed to militate against a statistical diagnosis of diarrhea in this age group. The comparisons among the various groups revealed fewer and smaller differences than the day-to-day comparisons. With regard to number of stools the bottle-fed babies had statistically greater numbers of stools than did the breast-fed babies regardless of feeding regimen, but only during those early days of life when it might be assumed that lactation had not begun. There were no differences between breast-fed babies on the two regimens studied. Bottle-fed babies on self-demand feeding had significantly greater numbers of stools than did those on scheduled feeding on two days. With regard to variability, bottle-fed babies on self-demand feeding were most variable in number of stools per day. Breast-fed babies on self-demand feeding were next most variable and bottle-fed babies on strict scheduling were least variable.

VOLUME AND ACIDITY OF THE GASTRIC CONTENTS IN THE UNFED NEWBORN INFANT. JOHN THOMSON, Arch. Dis. Childhood **26**:558 (Dec.) 1951.

The acidity of gastric contents of the unfed newborn infant was investigated in 154 single infants and in seven sets of twins. The birth weight range of the singletons was over 4½ to 10½ lb. (2,040 to 4,765 gm.) inclusive. No relationship was found to exist between the birth weight of the 154 infants and the volume of the specimens recovered, the pH of the specimens,

or the incidence of achlorhydria. In 115 infants, 74%, free hydrochloric acid was present. No relationship was found between the birth weight of this group of infants and the volume of the free acidity expressed as milliliters of N/10 HCl in 100 ml. of gastric contents.

The presence of free hydrochloric acid is recorded in two singletons in the birth weight group of 3 to 3½ lb. (1,360 to 1,590 gm.) inclusive.

KELLY, Milwaukee.

AMEBIASIS IN A NEWBORN INFANT. GUILLERMO REPETTO, Rev. chilena pediat. **23**:357 (Aug.) 1952.

A 46-hour-old infant presented a dysenteric picture which after parasitologic examinations proved to be of amebic origin. At delivery its mother had the same symptoms, but the etiology could not be detected in spite of various parasitologic and rectoscopic examinations. Review of the literature shows that this infant is the youngest patient with amebiasis ever reported.

FROM THE AUTHOR'S SUMMARY.

Acute Contagious Diseases

MILD SCARLET FEVER. J. MEDIR, Arch. Pediat. **11**:545 (Mar.-Apr.) 1952.

During the last four years, a large number of children in Spain have had a mild form of scarlet fever which was frequently undiagnosed until desquamation and/or development of glomerulonephritis. This experience follows the trend of scarlet fever as reported in other countries.

The descriptions of the old classic textbook picture and that found clinically, at the present time, are given. Reasons for these changes may be the improved hygiene and nutrition of children, attenuation of the responsible Streptococcus, or the use of antibiotics in respiratory infections. Treatment with penicillin and gamma globulin is advised.

The bibliography includes reports from Spanish, Portuguese, Italian, German, and English language sources.

ALLEN, San Francisco.

EVALUATION OF RED CROSS GAMMA GLOBULIN AS A PROPHYLACTIC AGENT FOR POLIOMYELITIS: 1. PLAN OF CONTROLLED FIELD TESTS AND RESULTS OF 1951 PILOT STUDY IN UTAH; 2. CONDUCT AND EARLY FOLLOW-UP OF 1952 TEXAS AND IOWA-NEBRASKA STUDIES; 3. PRELIMINARY REPORT OF RESULTS BASED ON CLINICAL DIAGNOSES. W. McD. HAMMON JR., L. L. CORIELL, J. STOKES, P. F. WEHRLE, and C. R. KLIMT, J. A. M. A. **150**:739 (Oct. 25) 1952.

This is the preliminary report of a large field study of three epidemic areas made in the summer of 1951 and 1952. A total of 54,772 children, aged 1 to 11 years, received intramuscular injections; one-half of them received gelatin, and the other half immune globulin (approximately 0.14 cc. per pound [0.5 kg.] of body weight). Of the 27,386 children receiving gelatin, 64, or approximately 0.25%, contracted poliomyelitis. Of the other 27,386 children, receiving immune globulin, 26, or approximately 0.1%, contracted poliomyelitis. Many believe this to be statistically significant. Almost one-third of the children with poliomyelitis (28) became ill within a week of the injection and were equally divided between the groups receiving gelatin and immune globulin. The remaining two-thirds of the children (62) became ill from 1 to 10 weeks after the injections. Of these, 48 had received gelatin and 14 immune globulin. The severity in the individual cases is not considered in this preliminary report.

The authors do not state whether sufficient quantities of immune globulin will be available in the summer of 1953 to meet demands.

KIMBALL, Evanston, Ill.

COMPLICATIONS OF NASAL DIPHTHERIA TREATED WITH MASSIVE DOSES OF STRYCHNINE. P. GIRAUD, R. BERNARD, and P. ALLIES, Presse méd. **59**:609 (May 5) 1951.

Nasal diphtheria developed in a child of 6 years during convalescence from measles. Renal damage quickly appeared, shown by albuminuria and edema. Treatment was adequate with antidiphtheritic serum and large doses of penicillin. Tachycardia, which was considered to be due to a preceding rheumatic infection, was present. The electrocardiogram showed inverted T

and P waves in leads D II and D III. With salicylate treatment, the temperature subsided and the gallop rhythm disappeared. The following day purpura developed, and on the next day the boy had a clouded sensorium, a left facial paralysis, increased deep reflexes, and pharyngeal paralysis. The authors decided to try strychnine for this desperate condition, and, starting with small amounts, increased the dose rapidly to 150 mg. through the day. The dose was continued at this high level for 10 days, when tetanic spasms appeared. The dose was reduced, and the boy recovered totally.

DAFFINEE, Melrose, Mass.

CHANGES IN BACTERIAL FLORA OF THE MOUTH DURING ANTITOXIN-PENICILLIN TREATMENT IN CASES OF ACUTE DIPHTHERIA. K. CHOREMIS, M. NESTORIDOU, and P. DANELATOU, Ann. pædiat. **179**:250 (Oct.) 1952.

The changes in the bacterial flora of the mouth were examined in 29 cases of acute diphtheria in which treatment was with penicillin-antitoxin and in 27 cases in which treatment was with antitoxin alone. In the penicillin-antitoxin cases the Corynebacterium diphtheriae had completely disappeared in 10 days. The Gram-negative cocci were the most resistant of the remaining bacterial flora. In the cases in which antitoxin alone was used, the C. diphtheriae persisted in the mouth in 22.2% of the cases after 10 days' treatment. There were no great changes in the remaining bacterial flora.

FROM THE AUTHORS' SUMMARY.

ECZEMA VACCINATUM AND VACCINATION BY CONTAGION. L. CARTAGENOVA, Lattante **23**:552 (Sept.) 1952.

A 9-month-old boy with facial eczema was living with another infant, 12 months old, who had been recently vaccinated. A generalized vaccinia developed in the younger infant which was especially marked in the eczematous area. He became markedly toxic and hyperpyrexic, with a temperature of 104 to 105.8 F, and had a very rapid pulse and signs of bronchopneumonia. The patient was treated with oxytetracycline (Terramycin), 1 gm. daily, and with a salve containing chloramphenicol. The temperature fell by crisis on the third day. There was little residual scarring.

HIGGINS Boston.

ELECTROCARDIOGRAMS OF PATIENTS WITH POLIOMYELITIS. F. MULÈ and F. ANGELINI, Pediatria **59**:799 (Nov.) 1951.

Electrocardiograms were taken on 40 patients with acute poliomyelitis. Nine showed abnormalities indicative of myocardial injury. Repetition of the test during the convalescent stage revealed that the electrocardiograms of all nine patients had become normal.

HIGGINS, Boston.

SMALLPOX VACCINATION IN PREMATURE INFANTS. GUILLERMO REPETTO and RAUL ORTEGA, Rev. chilena pediat. **23**:350 (Aug.) 1952.

The authors, having reported in a previous paper on the very low proportion of infection among premature infants exposed to hospital contagion of smallpox (3 among 10), now study the effect on 83 premature infants given smallpox vaccination. They report that the reactions of the premature infant to smallpox infection and to vaccination are similar; those with higher birth weights (over 2,000 gm.) and the older infants were as highly susceptible (72%) as full-term newborn infants (76%), whereas those of lower birth weights or poor vital conditions were almost refractory (only 21.9% of "takes"). The authors did not observe any relationship between maternal immunity and the reaction of the infant to vaccination.

FROM THE AUTHORS' SUMMARY.

Acute Infectious Diseases

A STUDY OF THE PROPHYLACTIC VALUE OF CHLOROQUINE IN CHILDREN. HILDRUS A. POINDEXTER, J. Pediat. **38**:169 (Feb.) 1951.

Poindexter recommends chloroquine as a practical means of malaria control in tropical countries where other means of control are economically impossible. A dose of 0.3 gm. of

chloroquine phosphate may be given weekly by mouth to children as young as 2 years of age. In these small children, however, the initial dose should be 0.15 gm. given in the evening after a heavy meal. When dizziness occurs, an initial dose of 0.15 gm. may be given at bedtime for the first few weeks. If no further symptoms develop, the dose may be increased to 0.3 gm. within three weeks and then continued at that level.

MACDONALD, Pittsburgh.

RHEUMATIC FEVER TREATED WITH ACTH AND CORTISONE. J. D. KEITH and C. A. NEILL, Canad. M. A. J. **64**:193 (March) 1951.

Twenty-three patients with acute rheumatic fever were treated with corticotropin (ACTH) or cortisone. In all cases fever and arthritis were promptly relieved. Sedimentation rates returned to normal in most cases in three weeks. Three patients had nodules, which vanished in three weeks. Chorea disappeared in three weeks.

Cardiac findings were generally unchanged, although gallop rhythm frequently disappeared, and two patients with acute cardiac failure were dramatically improved when treatment was begun.

McGUIGAN Evanston, Ill.

EOSINOPHILIA INFECTIOSA. R. GOLDSTEIN, Ann. pædiat. **179**:216 (Oct.) 1952.

A syndrome is described after observation of one case and perusal of the literature. The illness started with pyrexia; leucocytosis, eosinophilia and eosinophile inflammation-like infiltration of various organs were observed. While Löffler's eosinophile infiltration of the lungs mainly affects adults, the present syndrome is chiefly found in children. The differential diagnosis against Hodgkin's disease, periarteritis nodosa and tropical pulmonary eosinophilia is easy, but parasitic diseases may produce similar signs in the visceral organs. On the other hand, the protracted course of the illness, the spontaneous tendency to get better, the febrile beginning, the absence of parasites and the occasional familial occurrence point to the infectious nature of the illness. In analogy with "infectious lymphocytosis" the author calls the syndrome "infectious eosinophilia."

FROM THE AUTHOR'S SUMMARY.

EFFECT OF UNIVERSAL CARBON-ARC LIGHT THERAPY ON THE DEVELOPMENT OF IMMUNITY. S. V. HEINLIF, P. Q. EDWARDS, K. E. FOGHT-NIELSEN, K. G. HANSEN, K. MAGNUS, and I. SCHEIBEL, Acta pædiat. **41**:415 (Sept.) 1952.

A firm biological foundation for the beneficial effect of treatment with carbon-arc light is still lacking. Based on the assumption of a protective effect against infection, the investigations reported in this paper concern the production of antibodies in children during treatment with universal carbon-arc light. Parallel control groups, treated with light of an indifferent ultraviolet content or with no light at all, were used in the studies. The formation of tetanus antitoxin after immunization with the usual prophylactic doses of tetanus toxoid could not be shown to be influenced by treatment with carbon-arc light. Neither was it possible to influence the tuberculin sensitivity of naturally positive persons, nor the development of local lesions and tuberculin allergy after vaccination with BCG. Attention is drawn to investigations concerning the neuromuscular system, physical capacity, and metabolic variations, as possibly being fruitful spheres for continued study, and strong emphasis is laid on the absolute necessity of accurate dosimetry in future scientific investigations concerning the biological effect of light.

FROM THE AUTHORS' SUMMARY.

Chronic Infectious Diseases

VACCINATION AGAINST TUBERCULOSIS BY MEANS OF DEAD BACILLI (VACCINATION PETRAGNANI-SALVIOLI: V.P.S.). B. RONDININI and G. LENZI, Pédiatrie **40**:927, 1951.

Infants were vaccinated with formol-killed bacilli during their first week of life. Observations over 11 years on 10,000 subjects showed a reduced morbidity and mortality among the immunized children. Also the morbidity from sources other than tuberculins was reduced in the vaccinated group. The Mantoux test was positive in 86% of the patients after 11 years, but other skin reactions due to antituberculous allergy did not show the same high incidence.

GLASER, Jerusalem.

INORGANIC PHOSPHORUS CONTENT OF SPINAL FLUID IN TUBERCULOUS MENINGITIS TREATED WITH STREPTOMYCIN. R. GARSCHE and F. SOUCHON, Ann. pædiat. **179**:239 (Oct.) 1952.

The inorganic phosphorus in the spinal fluid of children with tuberculous meningitis is usually increased. With streptomycin therapy the spinal fluid phosphorus decreases as a rule within three months, corresponding to the cure, but when the disease has a chronic course, the phosphorus level remains high for months and reaches values of over 5 mg. per 100 cc. There is a parallelism between the phosphorus and the protein contents of the spinal fluid which is particularly marked during the development of the hydrocephalus syndrome. It is assumed that the phosphorus originates in the brain tissue and increases in the spinal fluid during the process of cerebral atrophy.

AUTHORS' SUMMARY.

FAILURES OF BCG VACCINATION. J. VON DESCHWANDEN, Schweiz. med. Wchnschr. **82**:283 (March 15) 1952.

Of 46 German children who had been vaccinated with BCG one-half to two years before admission to an institution in Switzerland at an elevation of about 4,600 ft. (1,400 m.), 20 did not react to tuberculin. Further, 13 reacted weakly or very weakly. Relatively many had symptoms of a vaccination injury such as hilitis. After four months in this institution 10 of the 13 weakly reacting children responded to the tuberculin test with a definite and considerably stronger reaction. Four of the 20 nonreactors then reacted. The vaccination injuries improved rapidly. The reason for these failures to react after BCG vaccination is seen in the poor nutrition and the unhygienic conditions of life.

AMBERG, Rochester, Minn.

BEHAVIOR DISORDERS FOLLOWING TUBERCULOUS MENINGITIS CURED BY STREPTOMYCIN. M. SCHACHTER, Clin. pediat. **34**:435 (July) 1952.

There has been a tendency to overlook the more usual causes of maladjustment in children who have recovered from tuberculous meningitis and to ascribe the subsequent emotional behavioral and mental disorders to either the streptomycin or the brain damage from the meningitis.

A 5-year-old girl was brought to the attention of the author because she was unmanageable and delinquent; she had had tuberculous meningitis at the age of one year, been cured by streptomycin, but had been deaf ever since the illness. Examination revealed that the child had a normal mentality; the death of the father and a struggling, distraught mother, who did not understand the problems of a deaf child, really afforded the background for the personality difficulties. The child was sent to a school for the deaf.

HIGGINS, Boston.

SOME THOUGHTS AS TO TUBERCULIN ALLERGOMETRY. F. COPELLO, Lattante **23**:406 (July) 1952.

The use of only a single intradermal injection is necessary for a theoretically and fundamentally accurate evaluation of a person's allergy to tuberculin.

HIGGINS, Boston.

THIOSEMICARBAZONE IN PULMONARY TUBERCULOSIS OF CHILDREN. G. BONTEMPELLI and G. MAZZEO, Lattante **23**:513 (Sept.) 1952.

Twenty children, ranging in age from 3 to 11 years, were treated for pulmonary tuberculosis with thiosemicarbazone in relatively conservative doses. Of nine patients with hilar node involvement, clinical improvement was recorded in five of eight patients with exudative pulmonary lesions improvement was recorded in two, and of three with pleuritis improvement was seen in only one patient. The authors concluded that the drug had not given evident and encouraging clinical results, especially since its use must be limited by reason of its toxicity.

A concurrent laboratory study showed (1) a lowering of the sedimentation rate in all but 3 cases, (2) an increase in the serum albumin globulin ratio in 16 cases and (3) a tendency for the percentage of polynuclear neutrophiles in the blood smear to be diminished.

HIGGINS, Boston.

RESISTANCE TO TUBERCULOSIS. ARVID WALLGREN, Rev. españ. pediat. **8**:401 (July-Aug.) 1952.

Natural and acquired immunity to tuberculosis is discussed, beginning with the discovery that healed tuberculosis of cervical nodes in childhood gave protection against severe secondary tuberculous infections. Persons who had never had a cervical lesion acquired severer forms of pulmonary infections.

However, a natural immunity is of more importance in combating an infection at any stage of the disease than any form of acquired specific immunity. Natural immunity is developed over a period of generations and accounts for racial immunity or susceptibility.

The use of BCG is discussed; the author states that the work of various investigators on the nature of acquired immunity leaves many questions unanswered. The hemoagglutinins of Middlebrook and Dubas are always encountered in patients with tuberculosis and in those vaccinated with BCG, but there seems to be little relation between the titer and the amount of resistance to tuberculous infections.

Perhaps the immunity to tuberculosis is cellular rather than humoral. Perhaps the titer is too low, or the antibody activity is directed toward the allergic qualities of the bacillus or its products and is of little importance immunologically. Certainly the various skin tests are of more importance diagnostically than prognostically.

At most, acquired immunity may compensate for lack of natural immunity when there might be an overwhelming amount of infection otherwise.

ALLEN, San Francisco.

RENAL CHANGES IN CONGENITAL SYPHILIS IN THE INFANT. JORGE ROSSELOT, Rev. chilena pediat. **23**:325 (Aug.) 1952.

Attention is drawn to the rarity of syphilitic nephropathies in infancy, and the clinical and laboratory bases that justify their diagnosis are shown. The author insists that with some frequency, when syphilitic patients undergo a specific treatment, urinary or edema alterations of some magnitude are noticeable, which could represent the possibility of a renal lesion. It is shown that these phenomena may also be due to intercurrent infections, malnutrition that sometimes exists, or reactivation caused by chemotherapy.

In his experience with 40 patients with syphilis, 75% showed a urinary syndrome; the albuminuria was high in 8 patients and microscopic hematuria existed in 11. The author presents the case histories of five infants of less than 2 months, with symptoms of florid congenital syphilis, and with evident manifestations of renal lesions. The existence of glomerulonephritis is suggested in two cases, and of nephrosis in the other three. After treatment with penicillin or aureomycin, total or partial regression of the renal alterations was evident.

FROM THE AUTHOR'S SUMMARY.

PSEUDOPARALYSIS OF THE HANDS AND CONGENITAL SYPHILIS. EUCLIDES PELUFFO and HECTOR C. BAZZANO, Arch. pediat. Uruguay **23**:583 (Sept.) 1952.

Four cases are reported of newborn babies who had abnormalities in the ability to move hands and fingers, coinciding with symptoms of congenital syphilis. Antisyphilis treatment produced rapid disappearance of the pseudoparalysis of the hands. The authors state that the finding of this clinical symptom must make one think of the existence of congenital syphilis and look for other symptoms to confirm or exclude the diagnosis and submit the patients to antisyphilitic treatment. Previously it is necessary to exclude other local or general causes that can produce it such as congenital paralysis, obstetric trauma, and meningitis.

FROM THE AUTHORS' SUMMARY.

BCG REVACCINATION. FRIEDRICH LINNEWEH and HELMUT LUTHER, Monatsschr. Kinderh. **100**:83 (March) 1952.

The authors vaccinated 36 tuberculin-negative patients in a children's home, ranging in age from 3 to 16 years, with BCG and revaccinated them three months later. The revaccinated

group showed increased sensitivity to tuberculin in contrast to the group who received only one injection of BCG. Revaccinated children exhibited an accelerated reaction at the site of vaccination (Koch's phenomenon).

The authors hope that revaccination with BCG at short intervals confers not only increased allergy but also more protection against tuberculosis.

LIEUT. HARTENSTEIN, M.C., U.S.A.

Diseases of Blood, Heart and Blood Vessels, and Spleen

THORACIC VENOUS ANOMALIES. JESSE E. EDWARDS and JAMES W. DUSHANE, Arch. Path. **49**: 517 (May) 1950.

As judged from the literature intrathoracic venous anomalies other than those of the vena cava system are extremely unusual. This paper records two cases of unusual intrathoracic venous anomalies, reviews similar reported cases, and discusses the developmental basis of the vascular malformation. In each of the two cases reported, the subject was a newborn infant. In one there was congenital mitral atresia associated with premature closure of the foramen ovale and an anomalous vein which connected the left atrium with the left innominate vein. In the second case, all the pulmonary veins failed to connect with the left atrium. Instead they were joined to form a common venous trunk which entered the abdomen and terminated by joining the ductus venosus. The authors attempt to explain these anomalies on the maintenance of connections which in the embryo are temporary and which usually are lost in the adult. In the first case they believe that the embryonic capillary plexus about the left lung bud retained its connection both with the main pulmonary venous trunk and, at the same time, with the cardinal venous system. In the second case the authors assume that part of the capillary plexus which gave rise to the pulmonary veins maintained anatomic continuity with those capillaries which were destined to represent the blood supply of the esophagus. From the plexus a gross venous channel arose. The lower part of the common pulmonary vein they interpret as developing from the primitive vascular supply of the stomach; it is a gastrointestinal vein in its origin.

HAW CHAN, San Francisco.

EXPERIMENTAL ENDOCARDITIS WITH FIBRINOID DEGENERATION IN THE HEART VALVES OF RATS. B. J. CLAWSON, Arch. Path. **50**:68 (July) 1950.

The author produced endocarditis with fibrinoid degeneration experimentally in the rat in a relatively high percentage of cases by intracardiac injections of alpha or beta hemolytic streptococci (Str. viridans or Str. pyogenes). One of the anatomical types of vegetations produced was similiar to that seen in human rheumatic valvulitis. Another type was bacterial in nature. The development of either kind of endocarditis did not appear to depend on streptococcic hypersensitiveness as far as could be determined by an intracutaneous skin test. The incidence of endocarditis was less in animals with a high concentration of Streptococcus antibodies in their serums than in normal animals.

HAW CHAN, San Francisco.

COMPARISON OF ARTERIOSCLEROTIC LESIONS PRODUCED IN YOUNG AND OLD RABBITS BY FREEZING THE AORTA. DAVID BALDWIN, C. BRUCE TAYLOR, and GEORGE M. HAAS, Arch. Path. **50**:122 (July) 1950.

Local hypothermal arteriosclerotic lesions were produced in the aortas of 10 senile rabbits and compared microscopically with lesions similarly produced in young rabbits in a previous study. The results indicated that the senile vascular wall reacted differently, although the pattern of reaction was similar. The principal quantitative difference was in relation to the degree of intimal proliferation, which was very prominent in young animals but limited and often abortive in old animals. Heterotropic formation of cartilage and bone was seen in old animals, but only rarely encountered in young animals.

HAW CHAN, San Francisco.

PAROXYSMAL TACHYCARDIA. EDWIN P. SCOTT, J. Pediat. **39**:168 (Aug.) 1951.

Edwin Scott reports two infants under one month of age with paroxysmal tachycardia. Digitalis relieved the attacks. One infant who had recurrences was temporarily relieved by either digitalis or quinidine sulfate.

MACDONALD, Pittsburgh.

EFFECT OF SURGERY ON GROWTH OF PATIENTS WITH PATENT DUCTUS ARTERIOSUS. FORREST H. ADAMS and W. B. FORSYTH, J. Pediat. **39**:330 (Sept.) 1951.

Surgical correction of patent ductus arteriosus has a stimulating effect upon growth, especially if performed early in childhood. If operation is delayed until late childhood, this growth-promoting effect may be lost.

MACDONALD, Pittsburgh.

IDIOPATHIC THROMBOPENIC PURPURA IN CHILDHOOD. WILLIAM A. NEWTON JR. and WOLF W. ZUELZER, New England J. Med. **245**:879 (Dec.) 1951.

The authors' report is based on an analysis of 47 cases of idiopathic thrombopenic purpura in children whose ages ranged from 9 days to 11 years. Sixty per cent of the patients were children between 3 and 7 years of age.

There was no apparent predilection for either sex and no familial tendency. In additional contrast to this illness as it appears in adults, the disease was short and self-limited, only rarely deviating from a benign course. Infectious or allergic etiology could not be demonstrated, but the majority of cases occurred in the spring.

Bone marrow aspiration was done in 30 cases and 23 specimens were suitable for study. There was no definite and consistent finding, although most of the specimens of marrow showed immature megakaryocytes with lack of granular development and poor platelet formation. The degree of eosinophilia was not consistent.

Clinical manifestations were routine in general; two patients had hemorrhage into the central nervous system and five suffered from hematuria. Anemia was produced by the severe bleeding in some instances, whereas in others there was no change.

The authors surveyed the aggregate results of treatment, both surgical and conservative, and concluded that conservatism was indicated, splenectomy being reserved for cases of uncontrollable bleeding and chronic recurrent purpura.

WHEELOCK, Denver.

LEFT CORONARY ARTERY FROM THE PULMONARY ARTERY: THREE CASES, ONE WITH CARDIAC TAMPONADE. HELEN I. MCKINLEY, JEANNE ANDREWS, and CATHERINE A. NEILL, Pediatrics **8**:828 (Dec.) 1951.

Three cases of left coronary artery arising from the pulmonary artery in infants are reported, making a total of 35 cases now reported. One of these was apparently complicated by cardiac rupture, a sequence not previously reported, to the authors' knowledge.

The symptom complex is again reviewed in order to stimulate interest in earlier diagonsis.

Since eight cases of this anomaly have been reported in adults, one of whom lived to the age of 64, it is suggested that the life of the infant might be saved if the condition is diagnosed before irreversible myocardial changes have occurred.

The ideal treatment, if vasodilator drugs fail, would seem to be a direct anastomosis of the left coronary artery with the aorta; however, since technically this is impossible at the present time, other methods of increasing the flow to the left coronary artery should be attempted. Gasul suggests the Potts-Smith operation, which, by raising the pulmonary pressure, might increase this flow.

FROM THE AUTHORS' SUMMARY.

LEUKEMIA IN CHILDREN. C. L. RODGERS, W. L. DONOHUE, and C. E. SNELLING, Canad. M. A. J. **65**:548 (Dec.) 1951.

The authors present a summary of cases of leukemia seen in a 16-year period prior to December, 1947, as a basis for comparison with cases in which the folic acid antagonists were

used. There were 148 cases. Over 90% of the patients had the acute fulminating type of leukemia, with average total duration of the disease of less than three months. About 7% of the cases were subacute, with duration more than twelve months. No case of chronic lymphatic leukemia was encountered. There were no apparent results from any therapy used.

McGUIGAN, Evanston, Ill.

ACTH AND CORTISONE IN THE TREATMENT OF LEUKEMIA. D. G. CAMERON, S. R. TOWNSEND, E. S. MILLS, and W. H. MATHEWS Canad. M. A. J. **65**:552 (Dec.) 1951.

Nine patients with acute leukemia were treated with corticotropin (ACTH) or cortisone. Three had no other therapy, the others receiving transfusions and penicillin as well. Four of these also received folic acid antagonists.

There was clinical improvement in all patients while receiving the hormones, though not necessarily associated with hematological remissions. Remission did not occur in any patient receiving hormones alone, and occurred in only one patient receiving transfusions and penicillin. All patients died. The authors do not see any benefit from the use of these hormones.

McGUIGAN, Evanston, Ill.

FOLIC ACID ANTAGONISTS IN THE TREATMENT OF LEUKEMIA IN CHILDREN. BERNARD LASKIM, J. M. M. DARTE, C. E. SNELLING, and WILLIAM DONOHUE, Canad. M. A. J. **65**:556 (Dec.) 1951.

Fifty-three cases of leukemia were treated with folic acid antagonists. In 37 this was the only specific therapy used. In 16 these drugs were used prior to or subsequent to corticotropin or cortisone. In no case was a permanent cure obtained, but in 26% there was a complete or partial remission of short duration with some prolongation of life. The authors found a high incidence of toxicity which was transient in nature. Aminopterin (4-aminopteroylglutamic acid) and Amethopterin (4-aminomethylpteroylglutamic acid) were used, with no apparent difference in results.

McGUIGAN, Evanston, Ill.

ACTH AND CORTISONE IN TREATMENT OF LEUKEMIA IN CHILDREN. J. M. M. DARTE, C. E. SNELLING, B. LASKI, S. H. JACKSON, and W. L. DONOHUE, Canad. M. A. J. **65**:560 (Dec.) 1951.

Thirty-seven cases of leukemia were treated with corticotropin (ACTH) or cortisone. All cases were acute. Nineteen patients had one or more temporary but complete remissions. Four had incomplete or partial remissions, and 13 had no demonstrable results. In one case the disease was apparently aggravated.

It was the impression of the authors that the patients with low peripheral blood cell counts obtained longer remissions. Following relapse, response to treatment was either more sluggish or without result.

The authors feel that while corticotropin and cortisone do not produce permanent benefit they are a useful tool in further investigation of the disease.

McGUIGAN, Evanston, Ill.

MEGALOCYTIC DEFICIENCY ANEMIA CURED BY SMALL AMOUNTS OF FRESH ENDIVE. G. M. H. VEENEKLAAS, Arch. Dis. Childhood **27**:209 (June) 1952.

Four cases of megalocytic hyperchromic deficiency anemia are described, which occurred at the end of the first year of life. One of these patients had been fed exclusively on goat's milk; three had had a long-continued diet of cow's milk. All patients promptly and definitely recovered, with a reticulocyte crisis. Treatment varied; the first patient recovered with the addition of fresh vegetables and fresh fruit to the previous diet (1939); the second patient was cured by means of 200 gm. of fresh endive added to the preceding diet; the third patient received 100 gm. of endive with his diet, and the fourth patient received only 25 gm. of fresh endive with the same diet as he had before.

Fresh endive apparently contains substances which are able to cure megalocytic hyperchromic anemia. The folic acid content of fresh endive is 62 to 75 γ of folic acid per 100 gm. and its vitamin C content is 12 mg. The last patient received only 15 to 19 γ of folic acid and 3 mg. of vitamin C daily. The possibility that other substance contributed to this cure must be considered.

KELLY, Milwaukee.

BLOOD FORMATION IN INFANCY: PART II. NORMAL ERYTHROPOIESES. DOUGLAS GAIRDNER, JOHN MARKS, and JANET D. ROSCOE, Arch. Dis. Childhood **27**:214 (June) 1952.

The course of erythropoieses in a series of infants from birth to 3 months of age, has been defined, the marrow erythroid count being used as a measure of erythropoiesis.

Two factors are responsible for the changing red cell picture after birth: (1) changes in erythropoietic activity and (2) effect of body growth. There is no evidence that increased hemolysis is a significant factor.

Erythropoietic activity is governed principally by the arterial oxyhemoglobin level. From the age of 2 to 18 months the oxyhemoglobin is maintained constant at about 11 gm. per 100 ml.

In the fetus it is probable that erythropoiesis is also adjusted to maintain a similar level, of about 11 gm. of oxyhemoglobin per 100 ml.

FROM THE AUTHORS' SUMMARY.

ACUTE IDIOPATHIC HAEMOLYTIC ANEMIA. J. G. MILLICHAP, Arch. Dis. Childhood **27**:222 (June) 1952.

The diagnostic criteria of acute idiopathic hemolytic anemia are defined. Five cases of the disease occurring in children are reported, two of which showed autoagglutination at body temperature. One hundred seven case reports published since 1940 are analyzed, and the literature reviewed, with particular reference to cases in children. The significance of autoagglutination at 37 C. is discussed, and references to 10 cases of this disease, showing the phenomenon, are given. A negative Coombs test in two cases is reported, and the value of the test in differentiating the congenital and acquired types of hemolytic anemia is discussed. A recovery rate of 90% in children and 70% in adults is to be expected.

Spontaneous recovery may occur, but most patients require transfusion. A proportion of patients exhibiting continuing hemolysis, in whom transfusion is no longer practicable, may show a remission following splenectomy.

The etiology of the disease is briefly discussed.

KELLY, Milwaukee.

RUPTURE OF A MYCOTIC ANEURYSM OF THE THORACIC AORTA. S. N. JAVETT and E. KAHN, Arch. Dis. Childhood **27**:294 (June) 1952.

Fatal hemorrhage occurred in a child aged 2 years 7 months due to the rupture of an aneurysm of the aortic arch, probably mycotic in origin, into a bronchus of the upper lobe of the left lung. The etiology of aortic aneurysm in childhod is discussed, and the apparent predilection of mycotic aneurysm for the thoracic aorta is pointed out.

KELLY, Milwaukee.

LEUCOCYTE COUNT OF CHILDREN IN HOSPITAL. F. DRAPER, Clin. Rep. Adelaide Child. Hosp. **2**:62 (May) 1951.

In a brief discussion the author gives the normal leucocyte values at varying ages and lists the causes of abnormal leucocyte counts.

MCGUIGAN, Evanston, Ill.

COOLEY'S ANEMIA. O. E. BUDTZ-OLSEN and C. R. WOOLF, South African M. J. **26**:49 (Jan. 19) 1952.

Cooley's anemia occurring in several members of a Cape Town colored family is described, and the genetic aspects discussed. It is believed to be the first colored family in South Africa to be so studied.

MCGUIGAN, Evanston, Ill.

ARTERIAL GRAFTS IN THE SURGICAL CORRECTION OF CONGENITAL HEART MALFORMATIONS. P. SOULIÉ, M. SERVELLE, A. BARBEAU, O. SCHWEISGUTH and J. ROUGEULLE, Presse méd. **58**:761 (July 1) 1950.

The authors describe a graft of heterogenous vein sections in the course of performing a Blalock type of correction of congenital heart malformation. Four cases are presented in which such a graft was necessary because of a very short subclavian artery or an anomaly otherwise preventing direct anastomosis.

Three of the patients survived with satisfactory correction of their condition. The fourth died on the day following operation, as a result of extensive hemorrhage from the mouth and anus.

DAFFINEE, Melrose, Mass.

MEGALOBLASTIC ANEMIA WITH RELAPSES BUT WITHOUT ACHYLIA GASTRICA IN CHILDREN. E. NAJMAN and B. BRAUSIL, Ann. pædiat. **178**:47 (Jan.) 1952.

A case of megaloblastic anemia in a girl of 18 months is described. She suffered a relapse when she did not receive liver treatment. Free HCl was always present in the gastric juice; the secretion was reduced in the presence of intrinsic factor (Castle's test).

FROM THE AUTHORS' SUMMARY.

THE GASTRIC CHEMISTRY IN SUBCHRONIC ERYTHROBLASTOSIS AND IN COOLEY'S DISEASE AND ITS RELATION TO THE ACTION OF FOLIC ACID. R. CORDA and L. AZZENA, Ann. ital. pediat. **4**:528 (Dec.) 1951.

The authors have studied the gastric and duodenal chemistry in 18 children affected by Cooley's disease and subchronic erythroblastosis before and after the administration of folic acid.

To a nearly constant gastric hyposecretion corresponded a deficiency of the pancreatic endocrine function, both scarcely influenced by the administration of folic acid.

The authors draw the conclusion of the lack of specificity of gastric and pancreatic manifestations in these diseases on which folic acid, even on the erythropoietic side, did not produce any corrective action of the hematologic disorder.

FROM THE AUTHORS' SUMMARY.

HEMORRHAGIC DIATHESIS IN CHILD WITH GENERALIZED NONHEREDITARY TELANGIECTASIS. M. ORLANDELLI, Clin. pediat. **33**:561 (Sept.) 1951.

In a boy of 4½ years after an attack of measles, generalized telangiectasis developed over the thighs and later the abdomen; there was occasional bleeding. The case fits in with the descriptions of the Rendu-Osler-Weber syndrome, except that in this case the condition was not of a familial nature.

HIGGINS, Boston.

PAROXYSMAL TACHYCARDIA AND ITS SEQUELAE IN CHILDREN. LUCIANA SALMI, Clin. pediat. **33**:589 (Oct.) 1951.

Of 189 cases of paroxysmal tachycardia in children recorded in the literature, 49 were in infants under 2 months, 88 in infants under 1 year; 29 were in children between 1 and 3 years of age, and between 4 and 8 in each year group over 3 years of age.

Salmi reports four additional cases; in three of these the crisis originated in the ventricle, and in one in the auricle. One of the infants had a congenital heart lesion (Roger's disease), and an older child had rheumatic heart disease with involvement of both mitral and aortic valves. Some of the frequent electrocardiograms are reproduced in the article. In two of the children, definite electrocardiographic changes were found after the normal sinusoidal rhythm had returned.

HIGGINS, Boston.

DIAGNOSIS AND SURGICAL TREATMENT OF WERLHOF'S DISEASE. T. GROSSI, Clin. pediat. **34**:441 (July) 1952.

Five cases of Werlhof's disease are reported, in which splenectomy led to an immediate and lasting relief of the symptoms. It is the recurrent or chronic cases of idiopathic purpura in which splenectomy is indicated and successful; the basis for the differential diagnosis of these cases is outlined.

HIGGINS, Boston.

TRANSPOSITION OF THE GREAT VESSELS OF THE HEART. S. L. BIANCO, Lattante **22**:513 (Sept.) 1951.

The autopsy findings in the cases of 2 children with transposition of the great vessels are reported. In one of the children (aged 5 years), there were a patent interventricular septum, renal calculi and hydropyonephrosis. In the other child (aged 3 days), both the foramen ovale and the ductus arteriosus were open.

After a lengthy discussion of the pathogenesis of transposition of the great vessels, the conclusion is drawn that every case is peculiar unto itself in that the compensating mechanisms to allow oxygenation of the blood vary greatly.

HIGGINS, Boston.

TRANSITORY THROMBOASTHENIA. M. BERNARDI, Lattante **22**:680 (Nov.) 1951.

A 9-year-old boy had ecchymoses on the forearm, in the subclavicular region, and at the sites of the injections of rutin in the buttocks and thighs. There was a failure of the blood clot to retract. A blood smear revealed abnormally appearing platelets, which did not clump together. Recovery followed two transfusions. The thromboasthenia is believed to be due to a febrile grippal infection six weeks previously.

HIGGINS, Boston.

HYPOCHROMIC ANEMIA AND DIAPHRAGMATIC HERNIA. U. PELLIGRINI, Lattante **23**:392 (July) 1952.

A 6-year-old boy had several hospital admissions over a period of five years for hypochromic anemia. He also had a transdiaphragmatic gastric hernia. The anemia on each admission responded favorably to martial (iron) therapy and transfusions. Occult blood was constantly found in the stools. It appeared that chronic gastric bleeding was responsible for the anemia and that surgical treatment of the hernia would be necessary to prevent the frequent relapses of the anemia. Aside from the hernia and the anemia the child was in good health and well nourished.

HIGGINS, Boston.

A CASE OF A HEMORRHAGIC CONDITION PRESENT FROM BIRTH AND OF DOUBTFUL NATURE. A. M. CAVALLOTTI, Lattante **23**:413 (July) 1952.

A boy of 5 years had a family history negative for hemorrhagic disease, had bleeding from the umbilicus at birth, bleeding when the deciduous teeth were cut, frequent epistaxis, occasional crops of petechiae, marked hematomata when intramuscular injections were given, hemorrhage causing marked swelling of the hand, and a hemarthrosis of the knee. Various tests seemed to negate the diagnosis of hemophilia. The toluidine blue test indicated hyperheparinemia. Therefore 5 mg. of a 0.5% solution of toluidine blue per kilogram was injected daily for six days. This procedure was followed by a lowering of the coagulation time. No further hemorrhagic incidents had occurred one year later.

HIGGINS, Boston.

THE VALUE OF THE ELECTROCARDIOGRAM IN CONGENITAL CARDIAC PATHOLOGY. G. GRANATA and L. PARENZAN, Minerva pediat. **3**:491 (Sept.) 1951.

Although it is not possible in the majority of cases to make a complete diagnosis of a congenital malformation of the heart by electrocardiography, the deductions one can draw as to the equilibrium between the two ventricles and as to conduction mechanism can furnish valuable information which no other safe and simple method can give.

HIGGINS, Boston.

INTERAURICULAR SEPTAL DEFECT WITH LIGHT INTERMITTENT CYANOSIS AND INTENSE MURMUR; DISAPPEARANCE OF ALL SIGNS. AGUSTÍN CASTELLANOS, OTTO GARCIA, and HORACIO DE LA TORRE, Rev. cubana pediat. **23**:24 (Jan.) 1951.

A case is presented in which a girl was first seen at 4 months of age having intermittent cyanosis and attacks of dyspnea. She had a loud murmur in the second interspace to the left of the sternum, and angiocardiography showed both sides of the heart as well as the pulmonary

arteries and the aorta filled at the same time. At 5 years of age she had no murmur of any sort and no cyanosis, and results of angiocardiography were normal, revealing no abnormal passage of dye from the right to the left side. The authors present their concept of the mechanism involved in this picture.

NELSON, San Francisco.

ACUTE INFECTIOUS LYMPHOCYTOSIS WITH LESIONS OF ERYTHEMA MULTIFORME. JORGE E. HOWARD, Rev. chilena pediat. **22**:566 (Dec.) 1951.

The author reports a case of acute infectious lymphocytosis, with clinical manifestations of erythema multiforme, in a 2½-year-old child. No similar case was found in a review of the literature.

FROM THE AUTHOR'S SUMMARY.

ACUTE MONOCYTIC LEUKEMIA IN THE INFANT. JOSE LEGARRETA, CARLOS RIOS, and RAUL ERAZO, Rev. chilena pediat. **23**:345 (Aug.) 1952.

A bibliographic review of acute monocytic leukemia in children is undertaken. Two observations of this illness in children of 9 and 10 years of age are reported, with emphasis on the ulceronecrotic lesions of the mouth, the multiple hemorrhagic processes and the bone manifestations.

FROM THE AUTHORS' SUMMARY.

CLINICAL OBSERVATIONS OF PRIMARY MYOCARDIAL DISEASES OF INFANTS. E. KNOPF, Kinderärztl. Praxis **17**:294 (Sept.-Oct.) 1949.

Three cases are described in which infants under one year came to the hospital with symptoms of spastic bronchitis and died with symptoms of cardiac failure and in which the pathologic findings showed interstitial myocarditis with perivascular infiltration. A fourth patient recovered. Two further cases, in which infants died with cardiac symptoms after prolonged illness and with no apparent presence of infection in any other organ, are considered as possible instances of myocardial infection with a cardioatropic virus.

GLASER, Jerusalem.

THERAPY OF MORBUS WERLHOF IN CHILDREN. E. LORENZ and K. QUAISER, Wien. klin. Wchnschr. **64**:8 (Jan. 4) 1952.

Two girls, 10 and 14 years of age, are reported who presented the picture of a thrombopenic purpura. A 10-year-old boy, following a febrile respiratory tract disease, bled for a long time on slight injury of lips and nose. The thrombocytes were much reduced in number but increased to normal values on Stryphnon therapy (methylaminoacetopyocatechol), but a decisive improvement of the disease occurred after removal of chronic inflammatory tonsils from which pus could be expressed. This case represents a "symptomatic" thrombopenic purpura, in spite of its response to Stryphnon, while the first two cases represent an "essential" thrombopenic purpura. These did not respond to a number of recommended therapeutic procedures, but in the case of the 14-year-old girl there was response to tonsillectomy. The tonsils were cleft, and plugs could be expressed. The removal of the apparently normal tonsils in the other girl was followed by a transitory elevation of the thrombocytes, but the purpura yielded to a splenectomy. In none of the cases was a definite relation discernible between the number of thrombocytes and the purpura.

AMBERG, Rochester, Minn.

DIAGNOSIS OF BONE CHANGES IN LEUKEMIC CHILDREN BY THE AID OF X-RAYS. V. SVAB and B. HORAK, Pediat. listy **6**:335, 1951.

The authors have made a further examination of the x-rays of bones, particularly the metacarpals, in a total of 70 children with leukemia. Sixty-five had acute forms of leukemia, paramyeloblastic or micromyeloblastic, and the remaining 5 had chronic leukemia.

They found changes in the bones of an osteolytic rarefactory and proliferative nature in the well-known forms in more than 75% of the cases. Evidence of eccentric osteolysis, which is marked by an irregular narrowing or erosion of the cortex adjacent to the medullary canal,

and of rarefaction of the cortex was found in the metacarpal bones of all patients without exception. Changes were found in the metacarpal bones even of leukemic children in whom there was no clinical manifestation of bone or joint involvement.

In examining the films it is expedient to use a lens and to compare them with those of normal children of the same age.

The authors consider that leukemic changes can more often and more easily be found in the metacarpal bones than in the rest of the skeleton. These are in harmony with the anatomical status of the skeleton of leukemic children, since the disease is usually so advanced when it first becomes manifest that we should expect to find macroscopic bone changes which would be evident on the x-rays.

FROM THE AUTHORS' SUMMARY.

FALLOT'S TETRALOGY COMPLICATED WITH POLIOMYELITIS. D. KRATKOVA, Pediat. listy **6**:352, 1951.

A case of a boy of 1½ years suffering from Fallot's tetralogy complicated with poliomyelitis is described.

FROM THE AUTHOR'S SUMMARY.

CONGENITAL LEUKEMIA. L. PELIKAN and K. BARTA, Pediat. listy **7**:345 (Dec.) 1952.

Two cases of neonatal myeloid leukemia of the paramyeloblastic type are described, manifesting themselves in extensive skin infiltrations and one of them in tumor-like infiltrations of the viscera. In neither of them were the oft-cited congenital anomalies found. The mothers of both children are healthy.

FROM THE AUTHORS' SUMMARY.

Diseases of Nose, Throat, and Ear

ROENTGEN THERAPY IN LYMPHADENOSIS AND SINUSITIS IN CHILDHOOD, WITH 10-YEAR FOLLOW-UP OF 349 CASES. HAROLD LEVY, J. Pediat. **39**:223 (Aug.) 1951.

Levy states that infected and hyperplastic tonsils and adenoids should be removed by surgery when possible. There remains, however, a group of conditions of the nasopharynx in which x-ray therapy (not radium) is the treatment of choice. In general, x-ray therapy for treatment of infected or hypertrophic lymphatic tissue in the nasopharynx is indicated for very young children, for children with Eustachian tube obstruction, in sinusitis, when antibiotics have failed, in the child with cardiac or other chronic disease, in the "non-allergic" asthmatic patient, and in the presence of active infections or epidemics of poliomyelitis.

Levy advises small x-ray doses. In a large series of cases over a period of years he has had no ill effects from treatment. His results were good to fair in 88% of cases.

The treatment is controversial.

MACDONALD, Pittsburgh.

STUTTERING OF DIFFERENT TYPES OF IDENTICAL TWINS. FRIEDRICH S. BRODNITZ, J. Speech & Hearing Disorders **16**:334 (Dec.) 1951.

In a pair of identical twins, one showed all the symptoms of stuttering of long standing, while the second twin omitted whole words and had similar signs of an imitative type of stuttering. The coexistence of stuttering of different types in identical twins is a possibility that so far has been generally overlooked in research.

PALMER, Wichita, Kan.

Diseases of Lungs, Pleura, and Mediastinum

BRONCHOSCOPIC TREATMENT OF ATELECTASIS IN CHILDREN. B. GANS, Arch. Dis. Childhood **27**:254 (June) 1952.

Bronchoscopic aspiration in cases of atelectasis in children frequently leads to reexpansion of the collapsed lobe and therefore prevents bronchiectasis. Results are better when the collapse is due to an acute infection and less good if collapse results from pressure by glands on a bronchus. The general and local upset following bronchoscopy in children is slight.

KELLY, Milwaukee.

NOTES ON BRONCHOGRAPHY IN CHILDHOOD. MARY BURNELL, COLIN GURNER, H. D. SUTHERLAND, Clin. Rep. Adelaide Child. Hosp. **2**:76 (May) 1951.

Problems of bronchography in children are discussed briefly under the headings of preparation, x-ray technique, and anesthesia.

McGUIGAN, Evanston, Ill.

THE HEART IN THE CHILD WITH PNEUMONOPATHY. G. DE MURALT and H. P. MENANO, Helvet. paediat. acta **7**:623 (Dec.) 1952.

The authors studied the cardiac and circulatory disturbances resulting from diseases of the lungs in infants and small children. On the basis of 80 cases of bronchiolitis, atelectasis, interstitial pneumonia, bronchopneumonia, and pulmonary emphysema, the authors set up the clinical, roentgenologic, and electrocardiographic diagnostic patterns of the acute and chronic cor pulmonale of infants and small children. The different possibilities of evolution are illustrated by 10 typical examples. Treatment has to remove as quickly as possible the obstruction in the pulmonary circulation by administration of antispastics and bronchoscopic aspiration. Thus the appearance of a chronic cor pulmonale resulting from irreversible changes in the lungs may be avoided; the prognosis of chronic cor pulmonale is bad.

FROM THE AUTHORS' SUMMARY.

Diseases of the Gastrointestinal Tract, Liver, and Peritoneum

CONGENITAL ANOMALY OF THE ESOPHAGUS. L. TORRES MARTY and J. LLONA RAMIREZ, Arch. Pediat. **11**:547 (March-April) 1952.

The author reports a case of congenital dilatation of the esophagus in a newborn infant which simulated pyloric stenosis or spasm. These cases should be studied clinically, roentgenologically, and with an esophagoscope. This was done in this case, and x-rays and a picture of the stenosed muscles of the cardiac end of the esophagus are included. A 6 mm. esophagoscope was passed without difficulty. X-ray with barium confirmed the diagnosis. The stomach was greatly distended.

Treatment with human plasma and a suppository containing 3 mg. of papaverine and the esophagoscope was very effective. Vomiting ceased, and the child recovered rapidly and completely.

The author discusses the theories of the pathology in such cases. They are (1) the embryological theory of Meynert, (2) congenital malformations as described by Bord, (3) primitive cardiospasm, (4) primitive atony of the muscle, (5) phrenospasm, (6) gastrospasm, and (7) theory of achalasia. The difference between spasm and achalasia is that in spasm there is an active contraction, while achalasia is passive. Innervation is discussed, and the fact is mentioned that multiple congenital anomalies such as megacolon may coexist, although this was not true in the case reported.

Esophageal anomalies fall into three clasess: (1) anomalies of the esophagus alone, such as absence of esophagus, double esophagus, atresia, stenosis, and achalasia; (2) anomalies combined with tracheal malformation, including the tracheoesophageal fistula with or without atresia, and (3) anomalies in which other organs participate.

ALLEN, San Francisco.

ACUTE VIRAL HEPATITIS. HENRY F. KRAMER, Brooklyn Hosp. J. **9**:145, 1951.

Thirty-four cases of virus hepatitis were treated in the Brooklyn Hospital in a three-year period. Precautions to avoid transmission of the disease are discussed. Diagnosis and differentiation of the infections and of homologous serum types can be facilitated by early use of liver-function tests.

McGUIGAN, Evanston, Ill.

EFFECTS OF PROLONGED INFUSION OF THE DOG'S PANCREAS WITH GLUCOSE. E. M. BROWN JR., F. C. DOHAN, L. R. FREEDMAN, P. DEMOOR, and F. D. W. LUKENS, Endocrinology **50**:644 (June) 1952.

Severe hydropic degeneration of the islands of Langerhans and permanent diabetes have been produced in cats by repeated intraperitoneal injections of dextrose. The prolonged, sustained

hyperglycemia so produced was thought to be the most important factor in the production of the hydropic change and the persistent diabetes. To test further this possibility it seemed desirable to localize a sustained hyperglycemia to the pancreas or a portion of it. In this way the responses to systemic hyperglycemia might be avoided and changes found in the infused organ might be attributed to the local hyperglycemia. In the experiments reported herein, the successful infusion of a part of the pancreas with dextrose usually resulted in systemic hypoglycemia and in changes in the islands of Langerhans which include both hyperplasia and hydropic degeneration. Diabetes did not occur, nor was it expected, since only part of the pancreas was infused.

JACOBSEN, Buffalo.

CONGENITAL INTRINSIC OBSTRUCTION OF STOMACH AND DUODENUM IN NEWBORN. CLIFFORD D. BENSON and JOHN J. COURY JR., Harper Hosp. Bull. **10**:1 (Jan.-Feb.) 1952.

In the newborn infant, a prepyloric diaphragm was successfully treated; it was the second reported in the literature. Ten patients with congenital intrinsic obstructions of the duodenum were operated upon, with seven survivals. Of the group of 11 patients, 7 were premature and 2 of the deaths occurred in premature infants weighing less than 3 lb. (1,360 gm.) at the time of surgical intervention. With earlier diagnosis and surgical treatment, the prognosis of the infant with congenital intrinsic gastric and duodenal atresia is more favorable than formerly, even though the infant is premature.

FROM THE AUTHORS' SUMMARY.

PRELIMINARY REPORT OF USE OF NEW PLASTIC INTUBATION TUBE. ALBERT H. ANDREWS JR. and HOWARD S. TRAISMAN, J. Pediat. **39**:197 (Aug.) 1951.

The plastic feeding tube discussed has a trade name, Plexitron. The tube may be inserted via the nostril and left in place for days at a time.

MACDONALD, Pittsburgh.

ANTITHROMBIN TITER IN CYSTIC FIBROSIS OF PANCREAS. IRVING INNERFIELD, ALFRED ANGRIST, and JAMES W. BENJAMIN, J. Pediat. **39**:287 (Sept.) 1951.

Pancreatic trypsin production is reflected in plasma antithrombin levels. When trypsin production increases, antithrombin levels increase, and vice versa. Determination of antithrombin levels is therefore a relatively simple diagnostic test for pancreatic cystic fibrosis. Antithrombin levels are low in the severely ill young infant. The child with cystic fibrosis, from a few months to 1½ years, may have normal or high antithrombin levels. The child from 2 to 7 years, having survived infancy, but with a scarred poorly functioning pancreas, may have low normal or depressed antithrombin levels.

MACDONALD, Pittsburgh.

CONGENITAL BILIARY ATRESIA: REPORT OF THREE CASES, TWO OCCURRING IN ONE FAMILY. WILLIAM W. WHITTEN and GEORGE C. ADIE, J. Pediat. **40**:539 (May) 1952.

The authors review the history of biliary atresia from Aristotle to Adie. They report three new cases, two in siblings. The jaundice of congenital biliary atresia rarely appears at birth. It appears 4 to 15 days later and may vary in intensity from day to day. As the disorder continues, jaundice may become more intense and the color may change from dark-yellow to olive-green because of oxidation of bilirubin to biliverdin. Biliverdin produces no color in the van den Bergh test, and the icterus index is therefore a more reliable method for measuring biliary retention.

Generally speaking it is better to attempt surgery early. Two of the patients reported on recovered after the operation. In one of them, follow-up studies of liver function demonstrate the reversibility of hepatic damage.

MACDONALD, Pittsburgh.

USE OF BANTHINE [METHANTHELINE] BROMIDE IN INFANTILE COLIC AND VOMITING. HAROLD LEY and BEN M. ZWEIFLER, J. Pediat. **40**:570 (May) 1952.

The patients were infants with colic, vomiting, or both. The treatment consisted of use of methantheline (Banthine) bromide in doses of 5 mg. four times a day, usually dispersed into

a formula feeding. The drug was well tolerated. Results in 50 infants were as follows: 34 (68%) good, 6 (12%) moderately good, and 10 (20%) poor. Best results were obtained in cases of vomiting or colic accompanied with vomiting.

MACDONALD, Pittsburgh.

TREATMENT OF CONSTIPATION IN INFANCY AND CHILDHOOD. ALFRED J. VIGNEC and VIRGINIA C. MITTY, J. Pediat. **40**:576 (May) 1952.

Methylcellulose (Cellothyl) is effective in treatment of acute and chronic constipation in infants and children, particularly in the presence of spasticity with emotional factors. The treatment must be accompanied by high fluid intake.

MACDONALD, Pittsburgh.

INTUSSUSCEPTION—A REVIEW OF EXPERIENCE AT THE MASSACHUSETTS GENERAL HOSPITAL, 1937-1951. GEORGE HUGH LAWRENCE and HOWARD ULFELDER, New England J. Med. **247**:499 (Oct. 2) 1952.

The authors report a study of 53 cases of intussusception seen at the Massachusetts General Hospital in the 15 years between 1937 and 1951. Thirty-eight patients were children from 0 to 12 years of age and 15 were older, from 13 to 76 years.

The symptoms and signs differed somewhat according to the age. Intermittent and colicky pain was seen in most of the children and in all the older patients, whereas nausea and vomiting, a universal finding in the children, occurred in only half the adult cases. Melena was noted in only a few of the adults and in half the children. An abdominal mass was palpable in half the children and in a third of the adults. A rectal mass was felt in only six patients of the series, 4 of them in the younger age group. It is worth while to mention that 5 out of 6 of the very young patients apparently had no pain whatsoever.

Laboratory data was inconclusive, and more assistance was obtained from plain films of the abdomen which were taken in most of the adult cases and half the juvenile cases. Absence of a cecal gas shadow and suggestion of a soft tissue mass were helpful findings. Barium enema studies were frequently done.

The greatest delay in diagnosis and hence in definitive surgery occurred in adults because of the variations in the typical picture.

In the children there were 4 enteric and 34 enterocolic intussusceptions, a distribution which agrees with most other experiences. The adult cases are also divided according to location and the condition of the bowel.

No local cause for this disorder was found in 29 cases of the children, although a hypermobile cecum were found in 8 and mesenteric lymphadenopathy in 14. The authors also concluded from their observations that the location of the intussusception was a more important factor in determining gangrenous changes than the duration of symptoms.

The treatment at the Massachusetts General Hospital has been entirely surgical; the details of the 49 laparotomies are given. In 28 of the 36 younger patients so treated simple reduction was done with no deaths in the nongangrenous group.

In cases of gangrenous or irreducible intussusception resection and primary anastomosis were routine; details are given.

WHEELOCK, Denver.

PYLORIC STENOSIS IN MONOVULAR TWINS. GUY C. CUNNINGHAM and JAMES J. KELLY, South. M. J. **45**:75 (Jan.) 1952.

The authors report development of pyloric stenosis in each of monovulvar twins. Only 12 such instances are said to be reported in the literature. In the authors' patients symptoms began at the age of 8 weeks. Each twin was operated on; the Fredet-Ramstedt technic was employed. One infant died postoperatively, and the other recovered.

LOGAN, Rochester, Minn.

HEPATITIS AND NEPHROSIS DUE TO SOLUBLE BISMUTH. SAMUEL KARELITZ, and AARON D. FREEDMAN, Pediatrics **8**:772 (Dec.) 1951.

An instance of jaundice, abdominal pain and enuria due to administration of bismuth sodium thioglycolate (Thio-Bismol) with liver and kidney damage is reported. The great toxicity of the water-soluble preparation of this heavy metal in this and other similar cases is stressed.

Attention is drawn to the use of dimercaprol (BAL) therapy in the early or first phase, to the need for caution in fluid administration in cases of lower nephron nephrosis caused by bismuth during the anuric and oliguric phases, and to the need for covering the loss of fluid and electrolytes in the subsequent diuretic phase.

The use of soluble bismuth preparations should be limited to specific conditions and to those cases only in which there is failure to respond to less toxic drugs.

FROM THE AUTHORS' SUMMARY.

PSYCHOGENIC MEGACOLON MANIFESTED BY FECAL SOILING. STERLING D. GARRARD and JULIUS B. RICHMOND, Pediatrics **10**:474 (Oct.) 1952.

The results of surgical therapy in cases of aganglionic megacolon have tended to create the impression that all cases of megacolon can be benefited by surgery. The authors have described six patients in whom megacolon had a psychogenic origin; this type of megacolon has been previously described as "functional" or "idiopathic" and its psychogenic origin has not been clearly recognized. Psychogenic megacolon may be diagnosed by the following clinical findings without the necessity of a detailed psychiatric history: admitting complaint of fecal soiling, onset in the second year of life or later, infrequent use of the toilet for defecation, defecation in the standing or supine position, inhibition of the stool, periodic voluminous stools, absence of episodes of intestinal obstruction, a feces-packed rectum, absence of a spastic segment of rectum or rectosigmoid, determined by use of Neuhauser's fluoroscopic technique, and a relatively benign course so far as physical status is concerned.

A sharp clinical distinction is apparent when the following findings of the aganglionic group are considered: admitting complaint of constipation without fecal soiling, onset at birth or in the first few weeks of life, use of the toilet for defecation, defecation in the sitting position, pellet-like or ribbon-like stools, frequent episodes of intestinal obstruction, an empty rectum, and the presence of a spastic segment of rectum or rectosigmoid as determined by use of Neuhauser's fluoroscopic technique.

A small additional group of cases has been described by others in which megacolon is due to anatomic obstruction; these cases can usually be diagnosed by digital examination of the rectum.

The authors have classified the symptom of megacolon into three groups and have given them the following generic designations: psychogenic, neurogenic, and anatomic. Only the neurogenic and anatomic groups are benefited by surgery.

FROM THE AUTHORS' SUMMARY.

INTUSSUSCEPTION. R. M. WANSBROUGH and R. W. CRAM, Canad. M. A. J. **67**:307 (Oct.) 1952.

Five hundred and seventy-five cases of intussusception during the period from 1915 to 1950 at Toronto Children's Hospital were reviewed. Mortality rates were computed for periods from 1915 to 1929, from 1930 to 1939, and from 1940 to 1950. Rates for these periods were respectively 27.5%, 17.6%, and 5.2%.

Tabulation of cases by ages showed 1.2% under 3 months, 61.8% between 3 months and 1 year, 15.8% between 1 and 2 years, 15.6% between 2 and 6 years and 5.6% between 6 and 14 years.

In the past 10 years, of 105 cases in which there was operation within 24 hours of the onset of symptoms there were no deaths. The authors stress the importance of early diagnosis, and point out that there are many cases which may show only listlessness and a single episode of vomiting.

Reduction of operative mortality is due primarily to Wangensteen drainage, maintenance of fluid balance, and chemotherapy.

McGUIGAN, Evanston, Ill.

BILATERAL PHAEOCHROMOCYTOMA IN A 6-YEAR-OLD BOY. CATHERINE A. NEILL and GWEN SMITH, Arch. Dis. Childhood **27**:290 (June) 1952.

The authors report a case of bilateral pheochromocytoma in a 6-year-old boy who showed peripheral vascular changes and hypertension. They discuss the differential diagnosis from acrodynia. Early laparotomy in any similar future case is recommended in view of the diagnostic difficulties.

KELLY, Milwaukee.

THREE CASES OF SEVERE JAUNDICE. G. P. SORMANO, Lattante **22**:598 (Oct.) 1951.

Three fatal cases of epidemic infectious jaundice in children are reported. In two of the children cirrhosis developed, and in the third, acute yellow atrophy of the liver.

HIGGINS, Boston.

SEVEN CASES OF CONGENITAL HYPERTROPHIC STENOSIS OF THE PYLORUS IN INFANTS. M. RADICI, Lattante **23**:420 (July) 1952.

Each of seven infants with hypertrophic pyloric stenosis were treated surgically—Ramstedt operation—with an excellent postoperative recovery.

HIGGINS, Boston.

EVALUATION OF PANCREATIC EXOCRINE FUNCTION. LEA RIVELIS and A. A. GIUSSANI, Arch. argent. pediat. **36**:44 (July) 1951.

An extensive review is made of the various tests employed in the study of pancreatic function; in particular reference is made to the diagnosis of mucoviscidosis (cystic fibrosis of the pancreas).

PANOS, Galveston, Texas.

VALUE OF ABDOMINAL PUNCTURE IN DIAGNOSIS AND MANAGEMENT OF ACUTE PERITONITIS IN INFANTS. RAUL P. BERANGER, ERNESTO SOMOZA and TOMAS HYLARED, Arch. argent. pediat. **36**:167 (Sept.) 1951.

A ten-year experience in abdominal puncture for diagnosis and management of acute peritonitis is reported. Eighteen positive diagnoses have been made by this means. The technique is described; it is emphasized that the procedure is innocuous if the listed precautions are taken. Five brief case reports are cited in illustration.

PANOS, Galveston, Texas.

X-RAY AND ANATOMICAL OBSERVATIONS IN STENOSIS OF THE PORTAL VEIN IN CHILDREN. HELMUT KÖRVER and HARALD KÖNIG, Arch. Kinderh. **143**:82, 1951.

A case of stenosis of the portal vein in a 2½ year-old girl is described. Esophageal varices had been demonstrated by x-ray.

Splenectomy did not bring relief, and death occurred 12 months after the initial signs of recurrent gastrointestinal hemorrhages. The stenosis had developed after an old partial thrombosis of the portal vein, complete organization of the thrombus, and formation of collateral circulation.

The authors discuss the possibility of an artificial anastomosis between the vena lienalis or the vena mesenterica inferior and the vena renalis, combined with splenectomy.

GOTTSTEIN, Chicago.

RESECTION OF INTESTINES IN INFANCY AND CHILDHOOD. RUDOLF JONAS, Wien. klin. Wchnschr. **64**:253 (April 4) 1952.

The importance of a proper preparation before operation and proper treatment after it in conjunction with the pediatrician is emphasized. In order to combat dehydration the use of Darrow's solution is recommended, preferably by continuous infusion. Before operation penicillin and streptomycin are given. Two female infants and a boy nearly 13 years old had intussusception, necessitating a resection. In one case a girl 5½ years old, with lymphosarcoma-like tumor, and in another a boy about 3½ years old with torsion of a congenital megasigmoid, had to be subjected to resection. All recovered.

AMBERG, Rochester, Minn.

CORTISONE TREATMENT OF SKIN INVOLVEMENT, ACRODERMATITIS ENTEROPATHICA, IN A CASE OF CYSTIC FIBROSIS OF THE PANCREAS. JENS UGLAND, Acta pædiat. **41**:483 (Sept.) 1952.

A case is reported of a child with fibrosis of the pancreas presenting a picture resembling that earlier described in the disease called acrodermatitis enteropathica, and the possibility is

suggested that the latter disease is always due to pancreatic fibrosis. The previously reported cases seem to support this assumption. The patient was treated with cortisone with very good effect. A preliminary account of the use of cortisone therapy for celiac disease is also given. The results noted appear to be encouraging.

FROM THE AUTHOR'S SUMMARY.

PERFORATED DUODENAL ULCER IN A NEWBORN GIRL. E. TEN BRINK and J. L. KEYZER, Maandschr. Kindergeneesk. **20**:108 (May) 1952.

The case history is reported of a one-day-old girl with a perforated duodenal ulcer. This is the second case in the literature of a successful operation for ulcer in a newborn infant. The child was discharged in good condition.

FROM THE AUTHORS' SUMMARY.

Nervous Diseases

CEREBELLAR DISORDERS IN LAMBS. LUDO VAN BOGAERT, Arch. Path. **50**:36 (July) 1950.

The author describes a case of progressive cortical atrophy or abiotrophy in a lamb. This disease afflicts newborn lambs and is apparently inherited and due to a recessive gene. Signs of incoordination and hypotonia are present. This entity is found in Corriedale lambs in Canada and different breeds of lambs in Britain. The causal genesis is conjectural; it has been suggested that a metabolic or toxic disorder of the cerebellar neurons may occur at the time of fetal development of the lamb, when migration of Purkinje cells is nearly complete.

HAW CHAN, San Francisco.

TERRAMYCIN THERAPY FOR MENINGITIS. ARCHIBALD L. HOYNE and EMMANUEL R. RIFF, J. Pediat. **39**:151 (Aug.) 1951.

Hoyne and Riff treated 27 meningitis patients with Terramycin (oxytetracycline) exclusively. In 14 of these the meningitis was meningococcic, in 6 influenzal, and in 7 pneumococcic. One patient, with pneumococcic meningitis and bilateral pneumonia, died. All other reported patients recovered.

Oxytetracycline was administered as an initial intravenous dose to all patients, followed by oral therapy. There were practically no unpleasant drug reactions. Oxytetracycline may prove to be the ideal drug for combating meningococcic and influenzal infections.

MACDONALD, Pittsburgh.

DIPLOCOCCUS CRASSUS MENINGITIS. WILLIAM F. SCHNITKER, J. Pediat. **39**:221 (Aug.) 1951.

Diplococcus crassus is part of the normal flora of the nasopharynx. In rare instances it becomes a virulent organism. A case is reported of meningitis due to D. crassus. The patient was 6 years old. She recovered on treatment with penicillin and sulfadiazine.

MACDONALD, Pittsburgh.

TREATMENT OF MENINGITIS DUE TO HAEMOPHILUS INFLUENZAE. SIDNEY ROSS, E. CLARENCE RICE, FREDERIC G. BURKE, JOSEPH J. MCGOVERN, ROBERT H. PARROTT, and JOHN P. MCGOVERN, New England J. Med. **247**:541 (Oct. 9) 1952.

The authors present a study of 15 cases of Hemophilus influenzae meningitis treated with a combination of chloramphenicol and sulfadiazine in an effort to help simplify the complex treatment of this type of infection. It is still uncertain whether the use of one or two of the broad-spectrum antibodies can effectively and safely replace the present methods that usually involve streptomycin (with its possibly neurotoxic effects and poor permeation of the blood-brain barrier) and rabbit serum (with its potential for serum reactions and excessive cost).

Chloramphenicol was administered intramuscularly in the acute phase of the disease in the form of a microcrystalline suspension, the dose ranging from 100 to 150 mg. per kilogram per day on a four to six hour schedule. Therapy was maintained for an average of 10 days. Some local reaction in the muscle of the buttocks was observed but no toxic effects on the hemopoietic system were detected by frequent complete blood cell counts. Presumably no marrow biopsies were indicated.

Sulfadiazine was given to all 15 patients, but whether or not it was valuable was undecided. The dose was 0.30 to 0.40 gm. per kilogram per 24 hours during the acute phase and 0.15 to 0.38 gm. during the convalescent period. Blood levels of 10 to 15 mg. per 100 cc. were attained.

Thirteen of the 15 patients recovered after a febrile period ranging for one to eight days. Only one child had on discharge, abnormalities related to the meningitis, namely, transitory lower extremity weakness.

The authors believe their data, combined with that of others whose contributions are noted, indicate that chloramphenicol is effective alone in mild to moderate infections of this type. Whether sulfadiazine is needed in severe cases is as yet undecided.

WHEELOCK, Denver.

CONVULSIONS WITH HIGH FEVER. G. CALZETTI and G. BORGHI, Clin. pediat. **34**:473 (July) 1952.

Statistical and clinical data have been gathered from the records of the Pediatric Clinic at Bologna on the occurrence of convulsions in children who have a high fever. The combination of convulsions with high fever occurred in 2% of all patients and in 50% of all patients with convulsions. Eighty-two per cent of the cases occurred in children between the ages of 6 and 18 months; its occurrence was exceptional in children over 3 years old; 63% of the cases were in boys.

In 49% of the cases the apparent cause of the fever was in the throat or nasopharynx; in 16% in the lungs, and in 7% in the gastrointestinal tract; in 24% of the cases the cause for the fever was not found.

Sixty-five per cent of the convulsions occurred on the first day of the illness, 25% on the second day, and 10% later. In 85%, the temperature exceeded 39 C. (102.2 F.); and in 36%, 40 C. (104 F.). Forty-three per cent of the convulsions lasted longer than 5 minutes, 22% lasted 5 to 10 minutes, 17% lasted 10 to 30 minutes and 18% over 30 minutes. Seven per cent of the cases showed some postconvulsive paresis. None showed important changes in the cerebrospinal fluid. The electroencephalogram is usually normal. Prognosis is usually favorable.

HIGGINS, Boston.

SPINAL TUMORS IN CHILDHOOD. HANS HOFF and KLARA WEINGARTEN, Wien. klin. Wchnschr. **64**:220 (March 21) 1952.

Spinal tumors in childhood are infrequent. Of the 162 spinal tumors seen in the surgical clinic in Vienna in ten years, about 5% occurred during childhood. Nine cases are tabulated. Of these, two were observed by the authors before operation; the other seven were those of the surgical clinic. The age varied from 2½ to 16 years. Only four were less than 10 years old. The diagnoses were meningioma (two), neurofibroma (two), neurinoma, ganglioneuroma, hemangioma of the bones, hemangioblastoma, and dermoid cyst (each one). Often children with spinal tumors are treated by orthopedic surgeons for years. The clinical features are discussed. The majority of spinal tumors in children in early childhood are malignant.

AMBERG, Rochester, Minn.

INVESTIGATION INTO THE PYRUVIC ACID CONCENTRATION IN BLOOD FROM CHILDREN WITH CONVULSIVE FITS AND PETIT MAL AND AN ASSESSMENT OF THE SIGNIFICANCE OF MUSCULAR ACTIVITY ON PYRUVIC ACID ESTIMATIONS IN INFANTS IN GENERAL. CATO LODDING, Acta pædiat. **41**:406 (Sept.) 1952.

The pyruvic-acid concentration was estimated in blood from 20 children between the ages of 2 months and 13 years suffering from convulsive fits or petit mal; 25 patients between the ages of 6 weeks and 14 years with no tendency to convulsive fits or petit mal served as controls. A mean value of 1.43 mg. per 100 cc. was found in the convulsive-petit-mal group (extremes 0.86 and 2.08 mg. per 100 cc.), while in the control group the mean value was 1.30 mg. per 100 cc. (extremes 0.83 and 2.07).

In the patients over 5 years of age, who generally kept quiet during the sampling, normal mean values were found both in the convulsive-petit-mal group and in the control group. Those

under 5 years of age, who never were at rest during the sampling presented abnormally high mean values in both groups. The high pyruvic-acid values are probably attributable to the great muscular activity displayed by these infants during the venepuncture. Experiments were made which showed that in children even light muscular work produces a rather considerable rise in the pyruvic-acid concentration in blood. The conclusion is drawn that no significant difference is found between children with convulsive fits or petit mal and a control series with regard to the pyruvic-acid concentration in blood.

FROM THE AUTHOR'S SUMMARY.

Psychology and Psychiatry

CEREBRAL LESION AND SCHIZOPHRENIA IN CHILDREN. ELIS G. REGNÉR, Svenska läk.-tidning **47**:2627 (Nov.) 1950.

This is a report of three cases illustrating a probable connection between various kinds of cerebral damage and schizophrenic states in young children. The first case was that of a boy 5 years of age. Several cases of schizophrenia had occurred in both the father's and the mother's family. Shortly after birth, the boy had bouts of cyanosis. His development was retarded. From the age of 3 when he changed his behavior, he stopped talking, displayed stereotype movements of increasing intensity, and probably had hallucinations. The diagnosis was psychosis following cerebral lesions. The second case was that of a girl 6 years of age with healthy parents and siblings. The stepfather, a narcomaniac was brutal to the children. At 4 years of age, the girl grew more silent and later stopped talking altogether. She became markedly changed in her behavior, and introverted, displayed peculiar stereotype movements with her hands, started bedwetting again, masturbated, and probably had hallucinations; she also had periods of stupor and catalepsy. A neurological examination including an electro-encephalogram was noncontributory. Her intelligence quotient was 76. The diagnosis was catatonic psychosis. One year later she showed improvement and became more active and lively. The prognosis is uncertain. The third case was that of a boy aged 6. Siblings and parents are healthy. It was suspected that the patient had icterus gravis as a newborn. He began to talk at 1½ years of age. When 4 years old he had the measles, and 6 months later he suddenly stopped talking. He became stubborn, did not like to play with other children, and showed stereotyped uneasiness. The diagnosis was postencephalitic psychosis.

WALLGREN, Stockholm, Sweden.

Diseases of Genitourinary Tract

ACUTE GLOMERULONEPHRITIS IN CHILDHOOD: A STUDY OF THE LATE PROGNOSIS OF 27 CASES. HYLAND J. HEBERT, J. Pediat. **40**:549 (May) 1952.

Aldrich was convinced by his clinical observations that the overwhelming majority of children with acute nephritis recover completely. In this study, Hebert has traced a group of 27 patients who were originally seen by Aldrich and his associates 20 to 30 years ago. According to Hebert, Aldrich's observations were right.

MACDONALD, Pittsburgh.

PRECOCIOUS GROWTH OF SEXUAL HAIR WITHOUT OTHER SECONDARILY SEXUAL DEVELOPMENT; "PREMATURE PUBARCHE," A CONSTITUTIONAL VARIATION OF ADOLESCENCE. SAMUEL H. SILVERMAN, CLAUDE MIGEON, EUGENIA ROSENBERG, and LAWSON WILKINS, Pediatrics **10**:426 (Sept.) 1952.

At puberty there is usually a simultaneous increase in secretion of adrenal androgens and sex hormones of the gonads. The latter are controlled by pituitary gonadotropins. It is not known what causes increased production of androgen by the adrenals at adolescence. Variation in the pattern of sexual development described could be due to (1) increased sensitivity of sexual hair follicles to normal levels of androgen present during the preadolescent period or (2) premature increase in secretion of adrenal androgen before the pituitary gonadotropic mechanism becomes activated. A comparison with normal levels reported by Talbot suggests that possibly the patients show a slightly increased excretion in relation to age, although this may be due to

minor variations in technic. The fact that height and bone age are somewhat above average in most cases may also be in favor of a slightly increased secretion of androgen. Possibly both these factors play a role. Although 7 of 31 patients had varying degrees of mental defect, it is doubtful whether this had any etiologic role. Early growth of pubic hair probably occurs more frequently than is realized. Children who are otherwise normal for their age are not brought to a physician because of its presence. On the other hand, mentally defective children are brought because of their neurologic disorder and the growth of hair is a concomitant finding. There is no explanation for the fact that the condition is much more frequent in females than in males.

FROM THE AUTHORS' SUMMARY.

PHENYLKETONURIA WITH A STUDY OF THE EFFECT UPON IT OF GLUTAMIC ACID. L. I. WOOLF and D. G. VULLIAMY, Arch. Dis. Childhood **26**:492 (Dec.) 1951.

An account of the clinical and biochemical features of phenylketonuria is given and five cases are described, in two of which the patients were aged only 18 months.

Contrary to expectation, no alteration in blood phenylalanine was found to occur after administration of glutamic acid, though the total amount of phenylalanine and its breakdown products excreted in the urine was found to increase in all except one case.

No significant increase in intelligence was found after continued administration of glutamic acid in the two patients treated.

KELLY, Milwaukee.

NEW METHOD FOR DETERMINING THE PRESENCE OF AMINO ACIDS IN THE URINE COLORIMETRICALLY. S. LO BIANCO and R. BOISSONNAS, Lattante **23**:410 (July) 1952.

A method for the determination of amino acids in urine has been developed by the authors at the Institute of Organic Chemistry in Geneva. Urea is first removed from the urine by hydrolysis with urease. The urine is then concentrated, and salts are removed electrolytically. The amino acids are then extracted by a solvent and the color reaction with ninhydrin is compared (colorimetrically) with a similar reaction with known amounts of amino acids.

HIGGINS Boston.

EXTREME ACIDOSIS OF RENAL ORIGIN. GUSTAVO GORDILLO, Bol. med. Hosp. inf., México **7**:166 (April) 1950.

The patient was a 6-year-old boy with urinary infection due to a vesical lithiasis, which began four years before he was admitted to the hospital. The child was hospitalized in a comatose condition because of acidosis caused by a severe renal insufficiency.

The author points out the extreme degree of acidosis (8.3 volume per 100 cc. of CO_2, and pH 7.3). That situation was corrected with infusions of ⅙ M sodium lactate solution controlled by frequent CO_2 and pH determinations. Afterward, the vesical calculus was removed, and an evident renal insufficiency was verified. Attempts were made to catheterize the ureters, but the operation was successful only on the right side. The left ureter did not allow the passage of the catheter, probably because of congenital stricture.

The general condition of the patient and the renal functioning improved so as to permit the child to be sent to the outpatient department.

A brief description is given of the buffer systems of the acid-base equilibrium in the organism, of the main types of unbalanced equilibrium found, and of the laboratory tests that are necessary to complete the diagnosis.

The author explains the causative mechanism of acidosis in the present case as being a faulty renal filtration due to a lessening of the production of ammonia and an insufficient tubular reabsorption. A brief review is presented of the modern therapeutics for acidosis.

FROM THE AUTHOR'S SUMMARY.

THE AGE OF MENARCHE IN FINLAND. GRETA SIMELL, Acta pædiat. **41**:9 (July) 1952.

In order to determine the average menarche age of Finnish women, information on this subject was collected from different parts of the country. The data concerned 3,075 women and

girls, born during the years 1923-1933, both Finnish-speaking and Swedish-speaking people, belonging to different classes of society in the country and in towns. The conclusion reached was that the average menarche age in Finland in 1950 was 14.25 ± 0.03 years or 14 years, 3 months ± 11 days. Since the year 1882 the menarche age in Finland has fallen by 2.37 years, and since 1919 by 1.70 ± 0.03 years. The years of war (1939-1944) do not seem to have had any retarding influence on the menarche age of Finnish girls.

According to the author's material the menarche age of the Finnish-speaking girls was higher than that of the Swedish-speaking girls. The menarche age of the Finnish-speaking girls was 14.28 ± 0.08 years, or 14 years, 3 months, 11 days ± 29 days, and that of the Swedish-speaking girls 13.85 ± 0.09 years, or 13 years, 10 months, 6 days ± 32 days. The difference was 0.43 ± 0.13 years, or 5 months, 5 days ± 48 days.

Grouped according to the various tribes the data revealed no great differences.

According to the author's material the menarche of intellectual workers and their daughters appeared earlier than that of manual workers and their daughters. For the intellectual worker this age was 14.03 ± 0.04 years, or 14 years, 11 days ± 14 days, and for the manual worker 14.39 ± 0.04 years, 14 years, 4 months 20 days ± 14 days. The difference was 0.36 ± 0.05 years, or 4 months, 10 days ± 18 days.

Grouped according to place of residence women living in towns attained the menarche at the age of 14.08 years ± 0.03, and women in the country at the age of 14.46 years ± 0.04, or the former at the age of 14 years, 29 days ± 11 days, and the latter at the age of 14 years, 5 months, 16 days ± 14 days. The menarche of girls born and living in towns appeared earlier than that of girls born and living in the country.

It seems obvious that the place of residence had an influence on the appearance of the menarche. Compulsory change of place of residence proved to have no retarding influence on the development of puberty in Karelian girls.

The girls in whom menstruation became regular immediately after the appearance of the menarche were at the time of the menarche on an average 14.21 ± 0.03 years old, or 14 years, 2 months, 16 days, ± 11 days, and those whose menstruation was irregular after the appearance of the menarche were correspondingly 14.47 ± 0.09 years old, or 14 years, 5 months, 19 days, ± 32 days. Thus the age of girls whose menstruation was regular at the time of the menarche was 0.26 ± 0.07 years lower than that of girls with irregular menstruation.

Girls whose menstruation was painful had it earlier than girls whose menstruation was painless. According to the author's material it cannot be concluded from constitution, or from the relation of height to weight, in which of them the menarche will appear earlier, and in which later. Girls whose menstruation was painful avoided gymnastics during menstruation more often than girls with painless menstruation. The appearance of the menarche seems to have no influence on school achievements.

The menarche is not distributed equally among the different calendar months. Most menarches fell in June, then in January, and then in September and December. The month of birth is obviously a frequent time for the appearance of the menarche. The percentage in the month of birth was 11.96 ± 0.46. Psychic factors seem to have a great influence on the age at which the menarche appears.

FROM THE AUTHOR'S SUMMARY.

STUDIES ON HEREDITY AND ELECTROENCEPHALOGRAPHIC PATTERN IN ENURESIS. H. C. HELSBORG, Ugesk. læger **112**:256 (Feb.) 1950.

Of 26 children with enuresis, 19 had relatives with enuresis; in 6 of these enuresis occurred on both paternal and maternal sides of the family. Six patients had relatives with epilepsy. Electroencephalography did not disclose any spike-and-wave potentials, but in nine patients and five parents there was dysrhythmia. Electroencephalograms were taken four times during enuresis on two sleeping patients, and there was a change of frequency from 2 to 3 cps to 6 to 8 cps. Patients with familial predisposition to enuresis and those with dysrhythmia are probably more resistant to treatment.

WALLGREN, Stockholm, Sweden.

TORSION OF TESTIS. A. T. HAGENS, Nederl. tijdschr. geneesk **94**:3292 (Nov. 18) 1950.

A description is given of a successful operation on the torsion of the testis, which had occurred five hours earlier. The ligamentum testis and the mesorchium posterior were missing on both sides. Ten weeks later no signs of atrophy of the testis were present.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Ductless Glands; Endocrinology

INFLUENCE OF CASTRATION ON FASTING METABOLISM. CLARA M. SZEGO and ABRAHAM WHITE, Endocrinology **48**:576 (May) 1951.

The data which have been obtained reveal that castration in either male or female mice results in profound alterations of lipid and water metabolism in the liver before and during fasting. The rate of protein mobilization from the liver during fasting is apparently unaffected. The present studies indicate further that the degree of involution of lymphoid tissue, which normally accompanies total inanition, is inhibited markedly in the castrate animal. The data are discussed on the basis of the concept of an imbalance which may result in adenohypophyseal secretion as a result of castration (overproduction of gonadotropins), and of fasting (overproduction of adrenocorticotropin).

JACOBSEN, Buffalo.

EFFECTS OF PROPYLTHIOURACIL ON THE GROWTH OF YOUNG MALE GUINEA PIGS. MINA MACNAIR BROWN and WILLIAM F. YOUNG, Endocrinology **50**:600 (June) 1952.

Thiouracil or thiourea treatment of young rats resulted in dwarfing or growth retardation. In contrast to the effect on the rat, propylthiouracil administration affected young beagle puppies only by increasing the weight of the thyroid glands.

In this study on guinea pigs virtually no effect was noted. It is suggested as an explanation for the general lack of effect that the guinea pig maintained at an environmental temperature of 70 to 75 degrees F. requires only a low level of thyroid activity and therefore is not dependent on thyroid hormone for many vital processes including growth.

JACOBSEN, Buffalo.

METABOLIC AND TOXICITY STUDIES ON PARA-HYDROXYPROPIOPHENONE. CHARLES C. SCOTT, ROBERT L. KROC and NEIL R. STASILLI, Endocrinology **50**:607 (June) 1952.

Findings in these studies do not support the concept that *p*-hydroxypropiophenone inhibits pituitary gonadotropin and thyrotropin.

JACOBSEN, Buffalo.

PRODUCTION OF CORTICOIDS BY RAT ADRENALS IN VITRO. MURRAY SAFFRAN, BERNARD GRAD and MARGARET J. BAYLISS, Endocrinology **50**:639 (June) 1952.

This paper describes the formation of corticoids by rat adrenal glands in vitro and the stimulation of this formation by the addition in vitro of corticotropin. The amount of corticoids produced depends upon the amount of corticotropin added to the adrenal in vitro. Only relatively small amounts of corticoids were found in both gland and medium kept at 2 C. Therefore, there are no large stores of preformed corticoids in the adrenal. Corticotropin apparently acts by stimulating the formation of corticoids from precursors, rather than promoting the release of corticoids from the gland.

JACOBSEN, Buffalo.

INHIBITION OF THE CATABOLIC EFFECT OF ADRENOCORTICOTROPIC HORMONE (ACTH) IN RATS BY A DIET HIGH IN POTASSIUM CHLORIDE. JOHN E. WHITNEY and LESLIE L. BENNETT, Endocrinology **50**:657 (June) 1952.

It is well recognized that hyperadrenocorticism, whether spontaneous or induced by exogenous corticotropin, may be associated with a negative nitrogen balance and reduction of potassium concentration in blood and tissues. To what extent these phenomena of nitrogen and electrolyte metabolism may be interrelated is not clear although there are reports in the literature

which suggest that an interrelationship is present. Evidence is presented in this paper which indicates that when rats are fed a diet high in KCl the increase in urinary nitrogen excretion produced by corticotropin is inhibited.

JACOBSEN, Buffalo.

SALINE HYDRATION AND DIURESIS AFTER ADRENALECTOMY. WILLIAM R. BRISTOL and VICTOR A. DRILL, Endocrinology **50**:677 (June) 1952.

Animals in adrenal insufficiency, when hydrated orally with water, cannot excrete the water at a normal rate. A delay in excretion is also obtained when the water is administered as dextrose or 0.85% saline solution. Even the administration of desoxycorticosterone acetate or adrenal cortical extracts will maintain a normal response to hydration for only a short period of time. In the adrenalectomized animal receiving excess fluids, the syndrome of water intoxication will also easily develop. Adrenal steroids, particularly desoxycorticosterone acetate, will offer good protection against water intoxication, without, however, markedly increasing urine output. In the present study, adrenalectomized animals were hydrated not only with water and isotonic saline solution but also with various intermediate concentrations of sodium chloride. It was found, depending on the actual concentration of salt administered, that the untreated adrenalectomized animal may excrete urine at a normal rate.

JACOBSEN, Buffalo.

INHIBITION OF THE DIABETES ENHANCING EFFECT OF ACTH BY A DIET HIGH IN POTASSIUM CHLORIDE. CONSTANTINE M. GLAFKIDES, LESLIE L. BENNETT and ROBERT GEORGE, Endocrinology **50**:684 (June) 1952.

It has been shown that a diet high in potassium chloride will inhibit the increase in urinary nitrogen produced by corticotropin in normal rats. In view of this it seemed of interest to determine whether a diet high in KCl would inhibit the increase in glycosuria produced by corticotropin in diabetic rats.

It was found that such a diet when fed to diabetic rats with minimal or moderate glycosuria inhibits the increase in glycosuria produced by minimum effective doses of corticotropin.

JACOBSEN, Buffalo.

THE URINARY PHOSPHATE EXCRETION FACTOR OF PARATHYROID GLAND EXTRACTS: A HORMONE OR AN ARTIFACT? G. S. STEWART and H. F. BOWEN, Endocrinology **51**:80 (Aug.) 1952.

Two hypotheses have been advanced in explanation of the parathyroid hormone control over the level of ionized calcium in the tissue fluids. One is that the hormone induces a release of calcium by a direct stimulating action on the bones; chemical changes, as reflected by the varying concentrations of calcium and of phosphorus in the serum and in the urine are considered secondary manifestations. According to the other hypothesis, the hormone acts primarily on the electrolyte equilibria of the body fluids in such a manner as to increase their solvent power for bone salts; bone dissolution follows as a secondary phenomenon. In brief, the sequence of events is supposedly as follows: 1. The hormone acts on tissue fluid phosphate rendering it more readily excretable by the kidney. 2. Serum phosphate is thereby decreased, resulting in tissue fluid undersaturation with respect to some equilibrium constant regulating serum calcium and phosphate concentrations. 3. Solution of bone salts occurs, leading to an accumulation of calcium in the serum.

The findings of the experiments on dogs reported in this paper offer negative support only to the bone cell hypothesis in that they are in no way irreconcilable with it; however, they do appear irreconcilable with the chemical solution hypothesis, especially with regard to the primary importance of kidney function and tissue fluid phosphate.

JACOBSEN, Buffalo.

ACTION OF ASCORBIC ACID ON THE RESPONSE OF THE PITUITARY-ADRENAL AXIS IN THE GUINEA PIG. HABEEB BACCHUS, MELVIN H. HEIFFER, and NORMAN ALTSZULER, Endocrinology **51**:94 (Aug.) 1952.

Previous work indicated that ascorbic acid pretreatment of rats and of mice prevented the eosinopenia characteristic of the alarm reaction. Moreover, it was demonstrated that the eosino-

phile response of the ascorbic-acid-pretreated rat to epinephrine was similar to the response of the adrenalectomized rat to the same stressor. This paper reports data on experiments which were planned to determine whether the vitamin possesses some specific anti-epinephrine action, and whether the vitamin per se alters the hematologic relations. The results suggest that there is no specific antagonism to epinephrine. It is suggested that the vitamin probably prevented the release of adrenocorticotropin by the anterior pituitary.

JACOBSEN, Buffalo.

FURTHER STUDIES ON THE TREATMENT OF CONGENITAL ADRENAL HYPERPLASIA WITH CORTISONE: IV. EFFECT OF CORTISONE AND COMPOUND B IN INFANTS WITH DISTURBED ELECTROLYTE METABOLISM. JOHN F. CRIGLER JR., SAMUEL H. SILVERMAN and LAWSON WILKINS, Pediatrics **10**:397 (Oct.) 1952.

Three cases of congenital adrenal hyperplasia with disturbed electrolyte metabolism, followed for 14 to 20 months, have been reported in detail.

The effects of cortisone (compound E) and corticosterone (compound B) on the suppression of abnormal adrenals and on the electrolyte disturbance have been discussed. Cortisone produces more marked suppression of the adrenal overactivity (as measured by the urinary excretion of 17-ketosteroids) but less sodium retention than corticosterone. Both steroids, however, significantly improve the electrolyte abnormality.

The possible mechanism of action of cortisone on the electrolyte metabolism is discussed.

Suggestions concerning the therapeutic management of these patients are offered. The use of adequate NaCl without desoxycorticosterone acetate in the initial treatment is emphasized, since suppression of the adrenal with cortisone seems to alter materially desoxycorticosterone requirement. The final combination of therapy, however, must be decided in each patient individually.

FROM THE AUTHORS' SUMMARY.

CLINICAL RESULTS WITH INJECTIONS OF FRESH HYPOPHYSIAL GLANDS OF CALVES. V. DIETER MÜTING, Deutsche med. Wchnschr. **77**:390 (March 28) 1952.

Freshly obtained and finely ground pituitary glands of calves and occasionally of sheep were injected intramuscularly repeatedly. For instance, a pituitary dwarf received 10 glands over a period of three years, resulting in a gain of growth in length of 25 cm. In some cases of hypophysial dystrophy slow improvement of the metabolism was noted. Altogether five of seven dwarfs of different etiology responded to the treatment. A drawback is that now and then allergic symptoms are elicited. These responded well to antihistaminics and calcium. An anaphylactic shock was observed once.

AMBERG, Rochester, Minn.

Diseases of Muscles, Bones, Joints, and Lymph Nodes

CONGENITAL MYATONIA: CLINICAL STUDY OF SOME NEW OBSERVATIONS. P. VERGER, Pédiatrie **40**:367 (no. 3) 1951.

Six cases are reported and the entity of Oppenheim's disease is described. The author believes that there are two forms: one which may occur either immediately after birth or later and which affects mainly the respiratory muscles and leads to death after a few months; and the other, which is always noticed after birth, without respiratory disturbances, and which may lead to incomplete recovery. The author does not feel that there is any justification to classify Werdnig-Hoffmann disease as a separate entity.

GLASER, Jerusalem.

CONTRIBUTION TO THE ETIOLOGIC CONCEPT OF PERTHES' DISEASE. L. HOLLÄNDER, Helvet. paediat. acta **7**:573 (Dec.) 1952.

After a review of the literature concerning the pathological and etiological explanations of Perthes' disease, the authors discuss dysostosis enchondralis epiphysaria, diseases conditioned by endocrine causes, and dysplasia luxans coxae as the predisposing factors in Perthes' disease. Mechanical factors precipitate the disease.

FROM THE AUTHOR'S SUMMARY.

OBSERVATIONS ON AND COMPLICATIONS OF ACUTE HEMATOGENOUS OSTEOMYELITIS TREATED WITH PENICILLIN. U. GRAFF, Deutsche med. Wchnschr. **76**:1651 (Dec.) 1951.

The acute septic process of the initial phase of osteomyelitis can be overcome by penicillin in a few days. In some cases a real abortive form of this disease can result. Acute hematogenous osteomyelitis was seen in 35 children. Penicillin treatment may mask all typical signs of inflammation and may thus lead to errors in judgment with regard to diagnosis and with regard to actual cure. Since, locally, interference with the circulation can lead to lack of proper distribution of the drug, a cure by penicillin alone is not to be expected, and other measures have to be used also, such as removal of pus. Sufficient immobilization with plaster-of-paris bandage is stressed particularly.

AMBERG, Rochester, Minn.

Diseases of Eye

CONGENITAL CATARACT IN ALBINO RATS FED DIFFERENT AMOUNTS OF TRYPTOPHAN AND NIACIN. RUTH L. PIKE, J. Nutrition **44**:191 (June 11) 1951.

Pike noted that a 0.2% tryptophan supplement to an acid-hydrolyzed casein diet is insufficient for both the tryptophan and the nicotinic acid requirements of the pregnant rat. The addition to such a diet of 10 mg. per 100 cc. of preformed nicotinic acid permitted the resumption of normal metabolism in the fetal lens, but this level did not permit normal growth and proper liver function in the maternal organism. It would seem that the resumption of normal metabolism in the liver and of normal growth would require more tryptophan, more nicotinic acid, or possibly additional amounts of some other factor or factors which may have been lacking in the diet employed.

FREDEEN, Kansas City, Mo.

Cutaneous Diseases; Allergy

ACTION OF HISTAMINE AND ANTIHISTAMINIC SUBSTANCES ON THE ENDOTHELIAL CELLS OF THE SMALL CAPILLARIES IN THE SKIN. A. GEDEON MATOLTSY and MARGIT MATOLTSY, J. Pharmacol. & Exper. Therap. **102**:237 (Aug.) 1951.

The conclusions from this interesting work are, in part, as follows: When a solution of histamine was applied to the skin of rats and mice and india ink injected intravenously, the endothelial cells of the small capillaries phagocytosed the carbon particles in the treated area. The induced phagocytic function of the endothelial cells endured for 15 minutes. Phagocytosis could be reactivated in the same site by repeated application of histamine. The phagocytic activity is diminished by small concentrations of antihistaminic substance and inhibited by higher concentrations. The endothelial cells of the small capillaries in the skin traumatized by burning or freezing show similar phagocytosis.

PILCHER, Cleveland.

USE OF THE "LIQUORPUMPE" IN FEER'S DISEASE. H. R. WIEDEMANN, Helvet. paediat. acta **6**:518 (Dec.) 1951.

Three patients with severe acrodynia (Feer's disease) were treated cautiously with the *Liquorpumpe* (the term *Liquorpumpe* is used for the process of repeated aspiration and reinjection of the cerebrospinal fluid) introduced by Speransky. A few days after this intervention, a definite and almost immediate improvement was observed.

With all reserve, in consideration of the course of these cases and of the method as such, it appears justifiable to treat patients with severe and with chronic acrodynia with the *Liquorpumpe*. This treatment is particularly indicated when the diseases have proved resistant to other simpler forms of treatment. The *Liquorpumpe* provides a more energetic form of treatment for these disturbances of the vegetative nervous system in early childhood. Children as a rule tolerate it well.

FROM THE AUTHOR'S SUMMARY.

ACRODYNIA IN A TWO-MONTH-OLD INFANT. L. PERALE, Clin. pediat. **34**:460 (July) 1952.

In a 2-month-old baby, breast fed, the symptoms of acrodynia, usually seen in older children developed, rash, pain in the extremities, and loss of appetite. The blood pressure was normal. Treatment was with vitamin B_6; six weeks later, the child had completely recovered.

HIGGINS Boston.

CONTRIBUTION TO THE ETIOLOGY OF ECZEMA OF INFANTS AND YOUNG CHILDREN. K. NITSCH, Med. Klin. **45**:585 (May) 1950.

An intracutaneous skin test with acetylcholine solution is recommended to show an increased irritability of the parasympathetic nervous system in cases of eczema. The bleb is often much more extensive than in normal controls. With healing of the eczema, the reaction diminishes. The variations of the test in controls make it difficult to determine a normal reaction, but it is possible to compare reactions in the same subject. It should be possible to exercise an influence on the eczemas of infants and children by measures acting on the vegetative nervous system. Since a dysregulation of the sympathetic and parasympathetic nerves is probable, such measures should have a depressing action on both. It is concluded on the basis of clinical observation, therapeutic effects, and tests of vegetative regulation that the nervous system plays an important role in eczema. Positive skin tests with egg albumen and similar substances indicate only an increased irritability of the skin. In cases of unquestionably allergic phenomena, the vegetative nervous system exercises a determining influence. Without a constitutional or possibly acquired tendency of the vegetative nervous system toward "allergic reactions" the antigen-antibody reaction cannot elicit disease symptoms in all cases.

AMBERG, Rochester, Minn.

COMBINED TREATMENT OF MALIGNANT MELANOMAS OF THE SKIN. ST. WOLFRAM, Wien. klin. Wchnschr. **64**:241 (March 21) 1952.

The combined treatment of malignant melanoma of the skin consists of primary x-ray treatment, followed by thorough excision by cautery. This again is followed by intense x-ray treatment. Of interest here is the case of a 12-year-old girl. Since birth she had a dark nevus in the sacral region, which became irritated frequently. No evidence of the disease was seen until publication (one year). In other cases the results were good, although the author realizes that the time of observation (three years) is too short for final evaluation.

AMBERG, Rochester, Minn.

LUPUS ERYTHEMATOSUS DISSEMINATUS TREATED WITH ACTH. MATTS PEHRSON, Acta pædiat. **41**:478 (Sept.) 1952.

The author describes a case of lupus erythematosus disseminatus in a girl aged 11 years. Corticotropin (ACTH) in doses of 24 mg. daily for 12 days produced marked improvement, which, however, lasted only as long as the course of treatment was in progress.

FROM THE AUTHOR'S SUMMARY.

Surgery and Orthopedics

OPERATING TABLE FOR YOUNG INFANTS. C. MARSHALL LEE JR., Ann. Surg. **134**:1066 (Dec.) 1951.

Advances in fluid and electrolyte control and other forms of supportive therapy have made possible major operations on young infants which would have been regarded impractical 20 years ago.

Nearly all writers on the subject of pediatric surgery stress the importance of conserving body heat during operations on all young infants. Therefore the author decided to design a table to be used for operations on these small patients. He describes his table in detail. It is made of Monel metal and is portable. Ideal temperature is maintained by circulating water.

Armboards for intravenous fluids, stirrups, and anesthetist's screen are attached to the table. Two illustrations are given.

After a year's experience with the table, the author feels that it very well meets his requirements.

BANTIN, Omaha.

Miscellaneous

SHOE-FITTING FLUOROSCOPE AS A RADIATION HAZARD. LEON LEWIS and PAUL E. CAPLAN, California Med. **72**:26 (Jan.) 1950.

Tests of direct beam intensity and stray radiation from shoe-fitting fluoroscopes indicate a wide variability of exposure of patrons and salesmen, with some exposures far in excess of standards proposed for safe use of the apparatus.

The principal potential danger is interference with bone growth in children as a result of careless use or uncontrolled dosage of x-rays. Although less likely, there is also some possibility of excessive exposure of shoe salesmen in exceptional circumstances.

The growing probability of increasing use of ionizing radiations warrants vigorous governmental control or possibly elimination of procedures of questionable merit which involve public risk.

FROM THE AUTHORS' SUMMARY.

STUDIES ON THE MECHANISM BY WHICH SULFADIAZINE AFFECTS THE SURVIVAL OF THE MAMMALIAN EMBRYO. ALLAN D. BASS, CHESTER L. YNTEMA, WARNER S. HAMMOND, and MARJORIE L. FRAZER, J. Pharmacol. & Exper. **101**:362, 1951.

The authors' conclusion from this and previous work is as follows: "Sulfadiazine and Sulfamerazine reduce the percentage of deliveries when administered to pregnant mice. This effect is obtained when these agents are administered prior to the eighth day of gestation. Evidence is presented which suggests that high blood concentrations of sulfadiazine interfere in some way with the production or utilization of either the female sex hormone or the gonadotrophic hormones."

FROM THE AUTHORS' SUMMARY.

THE PHYSIOLOGICAL DISPOSITION AND CARDIAC EFFECTS OF PROCAINE AMIDE. LESTER C. MARK, HERBERT J. KAYDEN, J. MURRAY STEELE, JACK R. COOPER, IRVING BERLIN, E. A. ROVENSTINE, and BERNARD B. BRODIE, J. Pharmacol. & Exper. Therap. **102**:5, 1951.

Because of its central stimulatory effects, the cardiac antiarrhythmic action of procaine is limited to anesthetized subjects. The results of the study of procaine amide in animals and human beings indicate that this agent, among other drugs, has very valuable actions. The authors' conclusions in fact are that it is relatively stable in the human body, that it is rapidly and completely absorbed from the gastrointestinal tract, and that plasma levels in man decline only 10 to 20% in an hour. It is an effective agent in ventricular arrhythmias. It does not usually eliminate the arrhythmia in chronic auricular flutter and fibrillation, but merely slows the auricular rate. It is relatively nontoxic and may be used by vein. Untoward effects have not been seen with daily oral dosage maintained up to three months.

PILCHER, Cleveland.

PHYSIOLOGICAL PERFORMANCE FOLLOWING A HYPNOTIC DOSE OF A BARBITURATE. ROBERT E. GOODNOW, HENRY K. BEECHER, MARY A. B. BRAZIER, FREDERICK MOSTELLER, and RENATO TAGIURI, J. Pharmacol. & Exper. Therap. **102**:55 (May) 1951.

The authors have been studying the actions of narcotics and hypnotics for some time, and this short paper, seven pages long, should be given thoughtful study by every physician who uses barbiturates. This study was made on 30 young men after a study of their normal reactions. Half of them received 0.1 gm. of pentobarbital sodium and the other half received a placebo at 1:45 a. m.; the test period started at 6 a. m., continuing until 11 p. m. After five days the tests were repeated, those who had previously received the barbiturate receiving the placebo and vice versa. The conclusion from the tests made was that the effect observed at 6 a. m. diminished after breakfast but was found to continue in a highly suggestive (qualitative

trend) but not statistically significant degree until after 4 p. m., 14 hours after medication. However, prior to the experiment the subjects had been informed that they would receive a "pill" before going to bed each night and that one or both of the pills might contain a very mild dose of a sedative. At the end of the last test session each subject was asked to guess on which night he had received a sedative. Twenty of the subjects guessed the correct night; two guessed both nights; three guessed neither night, and five guessed the wrong night. Since responses were correct oftener than would occur by chance, it is concluded that the "morning-after" effect of the barbiturate was recognized by the subjects as well as demonstrated by the tests. The cues used by subjects in detecting the drug effect were various and difficult for them to describe. They generally included "greater difficulty in getting up" on the morning after ingestion of the drug, and "greater lassitude" and "drowsiness" during the day. Difficulty in performing the tests, however, was seldom reported. Indeed, several subjects expressed surprise when they were later told that their test performance had deteriorated after the barbiturate had been taken. Loss in critical judgment, although difficult to measure, was evident in the subject's surprise.

PILCHER, Cleveland.

SIMPLE AND MALIGNANT DISEASE OF CHILDREN. JOSEPH LANNON and J. KATZ, South African M. J. **25**:891 (Dec. 1) 1951.

One-hundred twelve cases of malignant disease in children, not including glioma, are discussed. Seventy-nine per cent of the patients were under the age of 7 years. Commonest sites were the retroperitoneal area, the hemopoietic system, the central nervous system, and the lymphoid tissues. In other cases the pleura, ovaries, thyroid, and adrenals were involved.

Simple tumors with a specific predilection for children are much commoner than malignant; except for dermoids and tumors of the blood vessels, they tend to occur after the age of 7 years. Commonest are rectal polyps, hemangiomata, and lymphangiomata.

McGUIGAN, Evanston, Ill.

RELATIVE MERITS OF VARIOUS TECHNIQUES OF ANESTHESIA IN CHILDHOOD. GENEVIÈVE DELAHAYE, Presse méd. **59**:541 (Apr. 21) 1951.

The author discusses the physiological variants in childhood which make pediatric anesthesiology different from adult anesthesiology. She describes situations demanding various methods of anesthesia and points out the advantages and disadvantages of each.

DAFFINEE, Melrose, Mass.

News and Comment

ANNOUNCEMENTS

Pediatric Conferences.—The Universtiy of California Medical School, Parnassus & Third Aves., San Francisco, will hold pediatric conferences from June 22 through June 26, 1953. The fee will be $50. Correspondence should be directed to Stacy R. Mettier, M.D., Head of Postgraduate Instruction, Medical Extension, University of California Medical Center, San Francisco 22.

Seventh International Pediatric Congress.—The Seventh International Paediatric Congress is to be held in Habana, Cuba, Oct. 12 to 17, 1953.

It is proposed that a Symposium on Child Health in the Tropics should be held in Jamaica immediately after the International Congress, that is, Oct. 20 to 27, inclusive. This is to be held at the University College of the West Indies, Mona, St. Andrew, Jamaica, B. W. I.

The provisional agenda includes the following sections: (*a*) Nutrition; (*b*) Liver Disease; (*c*) Food Poisoning in the Tropics; (*d*) Infectious and Parasitic Diseases; (*e*) Prenatal and Neonatal Paediatrics; (*f*) Organization of Child Health Work in Underdeveloped Areas; (*g*) Miscellaneous.

As accommodation is limited, those wishing to attend are asked to communicate with the provisonal committee as soon as possible, sending preliminary notes on the papers they would care to present. Papers should be in English.

A list of hotel accommodations will be sent on request.

Communications should be addressed to:

The Secretaries, Symposium on Child Health,
Division of Medicine,
University College of the West Indies,
Jamaica, B.W.I.

Second Annual Clifford Sweet Lectureship.—Dr. Clement A. Smith of Boston will be visiting lecturer for the second annual Clifford Sweet Lectureship at Children's Hospital of the East Bay in Oakland, Calif., on May 20, 21, and 22.

Coming Examinations to Be Held by the American Board of Pediatrics, Inc.—The American Board of Pediatrics, Inc., will hold oral examinations on May 1, 2, and 3, 1953, in Philadelphia and on June 26, 27, and 28, 1953, in Ann Arbor, Mich.

Fifth Annual Morris Lamm Blatt Memorial Fund Lecture.—The pediatric staff of the Cook County Hospital announces that the Fifth Annual Morris Lamm Blatt Memorial Fund lecture will be given Monday, Oct. 26, 1953, in conjunction with the Julian Levinson Research Foundation. Dr. Milton G. Bohrod, director of the clinical and pathological laboratories at the Rochester General Hospital, Rochester, N. Y., will speak on "Pathology of Allergy." The lecture will be presented at 8:30 p. m. in the medical amphitheater of the Cook County Hospital.

Special Course in Cerebral Palsy.—A special course in Cerebral Palsy, limited to physicians, will be given at the Cook County Graduate School of Medicine, from June 15 through 26, 1953, under the direction of Dr. M. A. Perlstein, of Chicago. Enrollment in the course is limited, and all applications should be sent directly to the Registrar of the Cook County Graduate School of Medicine.

PERSONAL

Faculty Changes at Boston University School of Medicine.—The Boston University School of Medicine announces several changes in the department of pediatrics. Dr. Martin J. English, after 22 years of service, has retired from his positions as professor and head of the department of pediatrics and chief of the pediatric service at the Boston City Hospital.

Dr. Eli Friedman has succeeded Dr. English as chief of the pediatric service at the Boston City Hospital.

Dr. David McL. Greeley, assistant dean at the Boston University School of Medicine, has been appointed as acting head of the department of pediatrics and director of pediatric teaching at the Boston City Hospital.

GENERAL NEWS

Specialists Certified by the American Board of Pediatrics, Inc.—The following physicians were certified as specialists by the American Board of Pediatrics, Inc., after examinations held at Memphis on March 27, 28, and 29, 1953:

Adams, George Carlisle, Fort Hood, Texas.
Barnes, George Randolph, Jr., Fort Dix, N. J.
Bevil, Harold Hester, Beaumont, Texas.
Breg, William Roy, Jr., Bound Brook, N. J.
Brendel, William Bernard, San Antonio, Texas.
Britt, Robert Lee, Evansville, Ind.
Brown, O. Wharton, Jr., New Orleans.
Craven, Joseph F., New Orleans.
Crawford, Lloyd V., Memphis.
Del Campo, Dante, Pecos, Texas
Donald, William David, Birmingham, Ala.
Duby, Clarence J., Morristown, Tenn.
Dudley, Edward A., Jr., Columbia, S. C.
Egan, Merritt H., Salt Lake City.
Eliot, Johan Wijnbladh, North Little Rock, Ark.
Exline, Albert L., Jr., Austin, Texas.
Fowler, Richard E. Lee, New Orleans.
Furman, Robert Ayres, Cleveland.
Griffith, J. Edwin, Jr., Fort Defiance, Ariz.
Hagler, Carl William, Quincy, Ill.
Hannah, George S., San Francisco.
Hart, Wayne, Kansas City, Mo.
Humphries, Joseph M., Birmingham, Ala.
Johnson, Norman J., Little Rock, Ark.
Jordan, Gilbert F., Jr., Wichita, Kan.
Kadison, Elmer R., Austin, Texas.
Kirsme, Thomas W., Marinette, Wis.
Knapp, Brace I., Salem, Ore.
Kravtin, Abraham Joseph, Columbus, Ga.
Lavecchia, Joseph V., Jr., Chattanooga, Tenn.
Lis, Edward F., Park Forest, Chicago Heights, Ill.
McElfresh, Arthur Edward, Jr., Birmingham, Ala.
Middleton, James Gibbs, Camp Chaffee, Ark.
Miller, Robert A., Chicago.
Miller, Theodore White, Pueblo, Colo.
Newsom, William Taylor, Oklahoma City.
Norman, John A., Fort Sill, Okla.
Ohtani, Roy R., Honolulu, T. H.
Paschal, Jarvis Dean, Albany, Ga.
Perret, Joseph Maxine, Jr., New Orleans.
Philips, Robert Nathan, Fort Sam Houston, Texas.
Richert, Ruth H., Santa Monica, Calif.
Riedel, Henry A., Beverly Hills, Calif.
Robinson, Norman John, New Orleans.
Ross, Charles D., Van Nuys, Calif.
Rothschild, Joseph A., Memphis.
Schrum, David, Houston, Texas.
Stahlman, Mildren T., Nashville, Tenn.
Stryker, Winfield, Lt., (MC), U. S. A. F.
Tabris, Julius Austen, Kansas City, Mo.
Tedone, Louis M., Camp Roberts, Calif.
Thiel, Stanley W., Mattoon, Ill.
Thornton, Melvin Lee, San Antonio, Texas.
Willeford, George, Jr., Harlingen, Texas.
Williams, Gordon F., Menlo Park, Calif.
Winter, Calvert J., Pineville, La.
Woolley, Clifton W., Memphis.
Wright, Sam Martin, Rochester, Minn.

Books

Diagnostic Manual in Speech Correction: A Professional Training Workbook. By Wendell Johnson; Frederic L. Darley, and D. C. Spriestersback. Price, $2.50. Pp. 221. Harper & Brothers, 49 E. 33d St., New York 16, 1952.

This book is a workbook for the training of students in the diagnosis of speech disorders. As such, it covers the forms used by most speech correctionists, regardless of their philosophical basis of work; therefore, it should be useful in most professional training institutions as a general projects workbook.

The Public Health Nurse and Her Patient. By Ruth Gilbert, R.N. Price, $3.75. Pp. 348. Harvard University Press, Cambridge 38, Mass., 1951.

For 11 years this book has held its place as a "must" on any bibliography for nurses. In revising it, Ruth Gilbert has enriched her original theme by incorporating new growth and new trends in both nursing and mental hygiene. With her background of training and experience in both public health nursing and psychiatric social work, the author is particularly well equipped to bring this material to print.

If a word may be used to characterize the book as a whole, integrating seems to be that word. From first to last the reader is aware of a skillful process which weaves the thread of mental hygiene into the fabric from which public health nursing is fashioned. Like the threads from other disciplines long since drawn upon to make the nursing profession stronger and more serviceable, mental hygiene, as such, loses its identity.

The book highlights the force and meaning of the undercurrents of feeling which ebb and flow in the relationship between the public health nurse in the teaching and helping role and the patient, and also between the nurse and her co-workers.

Since this book does represent a process more than a portrayal, of necessity it has an intangible quality. This is balanced by generous use of case illustrations and a well-rounded choice of reference material.

The value of the book seems to increase in proportion to the experience and knowledge of human dynamics which are brought to the reading. None the less, the nurse just entering the field of public health should find it heartening, since it eases the pressure to know all the answers and strengthens confidence in her ability to give real help by accepting and understanding the people with whom she works so that she can share her experience and knowledge with them in a truly productive way.

Not only public health nurses, but nurses in general and any other group working primarily with people, will find this interesting and profitable reading.

The Clinical Use of Fluid and Electrolyte. By John H. Bland, M.D. Price, $6.50. Pp. 259, with 75 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5, 1952.

This is an excellent monograph on body fluid and electrolyte, being applicable to all specialties of medicine. The first chapter deals with the basic fundamentals of fluid physiology, and each succeeding chapter is concerned with a specific phase of the same. Except for the section related to pediatrics, all discussion is relative to adults. This is exemplified by the chapters concerned with fluid and electrolyte in surgical patients, geriatrics, adrenal cortex failure, heart failure, and diabetes mellitus, to name only a few. There are also references to the effects of corticotropin (ACTH) and cortisone on body fluid.

The value milliequivalents is used routinely in this text, and a method of conversion from milligram per 100 cc. is discussed. Of special interest are the numerous diagrams that accompany each discussion. Here we have a graphic comparison of the constituents of the normal

extracellular and intracellular fluid compartments and the changes that occur in each pathologic state. To use the author's own words: "It is apparent that one cannot deal with problems of body water and electrolyte without thinking and diagramming the clinical situation in terms of milliequivalents. There can be no question that such patterns simplify an otherwise confusing, difficult and esoteric clinical problem. It is strange that physicians frequently resent this change, inasmuch as it renders easily understandable a previously puzzling problem."

An extensive bibliography is found at the end of each chapter.

The author stresses the importance of intracellular potassium, magnesium, and phosphate in electrolyte physiology. One cannot overemphasize the role played by potassium in metabolic acidosis and alkalosis and diabetic acidosis. This is displayed not only by the special chapter on potassium metabolism, but through the entire reading. There is also a table of potassium-containing foods.

Of special interest to the pediatrician is the discussion of fluid therapy in diarrhea, vomiting, and renal disease. In this chapter there is also noted the fluid therapy of burns, shock, and adrenal insufficiency. There are graphs to compare these abnormal states with the normal. It is brought to the reader's attention that the interstitial compartment of the infant is much larger than that of the adult, and that the intracellular compartment is much smaller by comparison.

Dr. Bland has written an excellent book on a very important and ofttimes confusing subject. It is a clearly- and well-written text. This book is most highly recommended to all practitioners of medicine, regardless of specialty. It should be read by all interns and residents as well.

Posture and Pain. By Henry O. Kendall, Florence P. Kendall, and Dorothy A. Boynton. Price, $7. Pp. 204, with 159 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1952.

This book provides a manual of diagnosis and treatment of posture problems which will be found useful by the medical profession and students and practitioners of physical therapy. It provides a rationale for physiotherapeutic methods which all too often are prescribed without much thought as to just why they help.

A wealth of photographs and diagrams is contained in this book which very adequately illustrate the common faults of posture, and the methods of testing the joints and muscles in their relation to posture.

The various postural faults which result in pain are identified and analyzed, and rational corrective procedures are presented, and, in nearly all instances, illustrated. Enough discussion is included so that a physical therapy student will understand the principles involved rather than simply memorize and follow directions.

This reviewer finds a number of things which warrant critical comment. Among these are the omission of scoliosis, as to both diagnosis and treatment, and the apparent disregard of the gluteus maximus muscles as important postural structures.

Especially commendable to pediatricians is the chapter on developmental factors and environmental influences affecting posture, which points out the normal childhood deviations from adult posture standards. The views on footwear are interesting but are not, in some particulars, in accord with the views of many authorities on this subject.

CORRECTION

Through an oversight, in the abstract of the paper given by Dr. Paul György at the May, 1952, meeting of the American Pediatric Society (A. M. A. Am. J. Dis. Child. **84**:482, 1952) purified fractions from human milk were described as "crystallized" products. The word "crystallized" should have been omitted.

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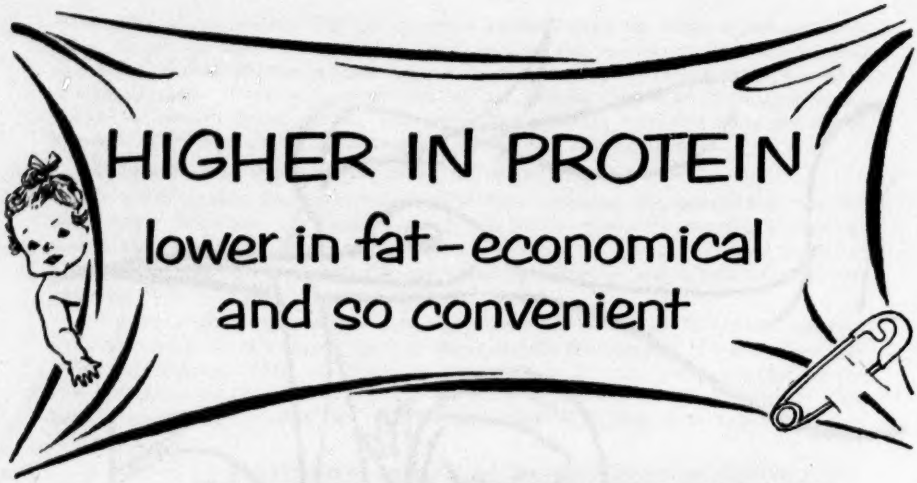

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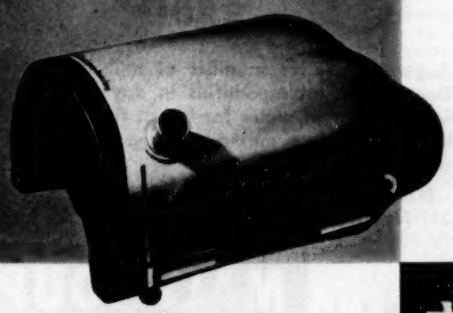

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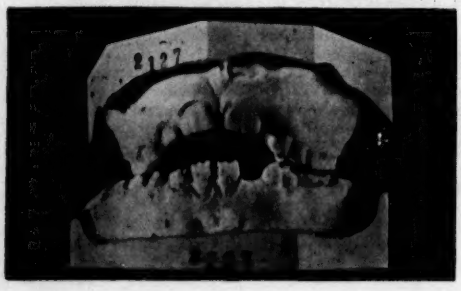

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Bibliography: 1. Vignec, A. J., and Mitty, V. C.: J. Pediat. *40*:576 (May) 1952. 2. Seidmon, E. E. P.: Am. J. Digest. Dis. *18*:274 (Sept.) 1951.

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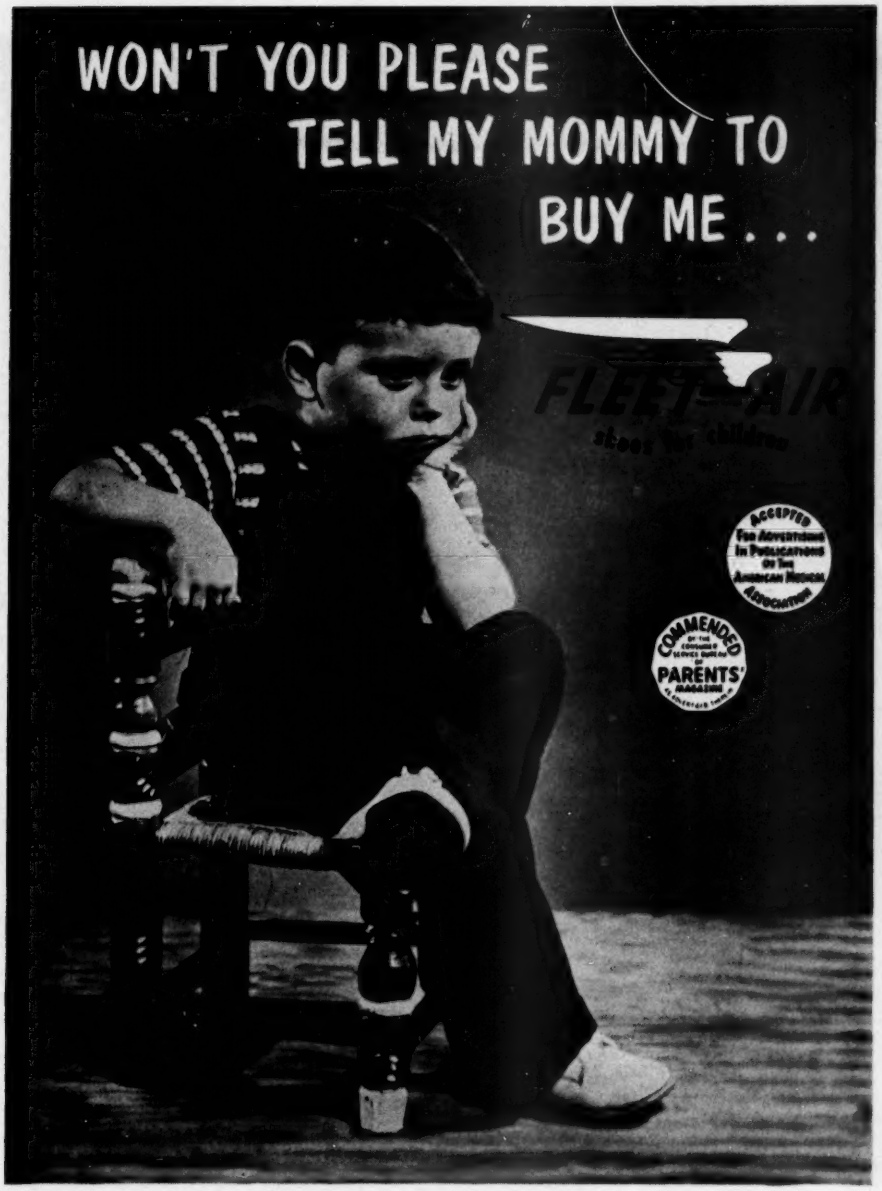

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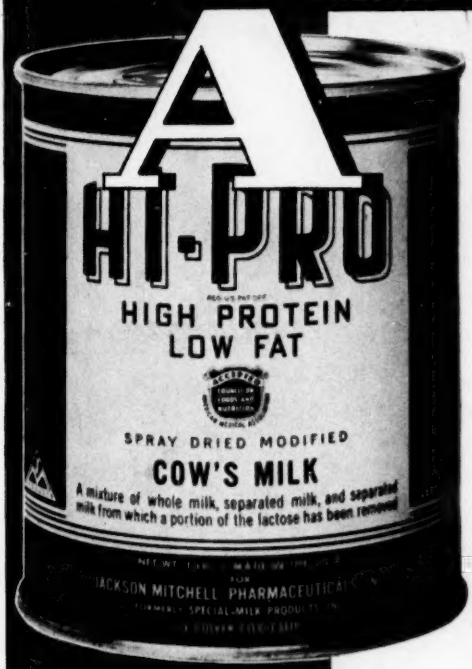
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Fat	14.0%	Calcium (Ca)	1.15%
Lactose	35.0%	Phosphorus (P)	1.65%
Minerals	6.5%	Potassium (K)	1.17%

Calories per oz.	121
Calories per tbsp.	40
Proteins per oz.	11.7 grams
Proteins per tbsp.	3.9 grams

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